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Tumor-Associated Antigens

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DETECTION/ CHARACTERIZATION/ ISOLATION

1. A NONFUNCTIONAL PROTEIN IN HUMAN LEUKEMIA CELLS REACTS WITH ANTISERUM TO DIHYDROFOLATE REDUCTASE FROM L1210 LEUKEMIA CELLS.

Iqbal MP, Rothenberg SP
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Life Sci; 29(7):689-696 1981

Antiserum raised in chickens to dihydrofolate reductase purified from L1210 leukemia cells by affinity chromatography inhibited the catalytic activity and the binding of methotrexate by the enzyme. Lysates of human chronic myelogenous leukemia cells, which had neither catalytic activity for dihydrofolate reductase nor binding of methotrexate, blocked the inhibiting effect of the antiserum on the function of the enzyme in L1210 cell lysates. In double immunodiffusion, these human leukemia cell lysates formed a single precipitin line against the antiserum. These findings indicate that nonfunctional dihydrofo

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late reductase in human leukemia cells share an antigenic determinant(s) with a functional form of the enzyme from L1210 murine leukemia cells. (Author abstract) (21 Refs)

2. A NOVEL HUMAN T CELL ANTIGEN PREFERENTIALLY EXPRESSED ON MATURE T CELLS AND SHARED BY BOTH WELL AND POORLY DIFFERENTIATED B CELL LEUKEMIAS AND LYMPHOMAS.

Kamoun M, Kadin ME, Martin PJ, Nettleton J, Hansen JA
Dept. Lab. Medicine, Univ. Washington SB-10, Seattle, WA, 98195
J Immunol; 127(3):987-991 1981

A new lymphocyte differentiation antigen shared by all normal T cells and some malignant B cells was defined by a monoclonal antibody designated 12.1. This antibody reacted with all peripheral blood T cells but not with normal B cells and B cell lines. Analysis with a fluorescence activated cell sorter showed that the expression of 12.1 antigen changes during T cell maturation. Most thymocytes, blasts of acute T cell leukemia, and cells from established leukemic T cell lines bear a small amount of 12.1 antigen. In contrast the majority of peripheral blood T cells, activated T cells, and leukemic T cells of the Sezary syndrome bear a large amount of 12.1 antigen. Unexpectedly, antibody 12.1 reacted with leukemic cells from most patients with B-type chronic lymphocytic leukemia (CLL) and some patients with lymphosarcoma cell leukemia (LSCL). Among these leukemias, expression of the 12.1 antigen was not correlated with the stage of B cell maturation, with the amount of surface immunoglobulin on the cells, or with the presence or absence of monoclonal gammopathy. In a comparative serologic analysis the antigen defined by antibody 12.1 was distinct from the p67 T cell antigen (defined by monoclonal antibody 10.2) that is also known to be expressed by B-type CLL cells. (Author abstract) (22 Refs)

3. BINDING OF MONOCLONAL ANTIBODIES TO HUMAN BREAST CANCER (MEETING ABSTRACT).

Hendler FJ, Yuan D, Vitetta ES
Departments of Medicine and Microbiology, University of Texas Health Science Center at Dallas, Dallas, TX, 75235
4th Annual San Antonio Breast Cancer Symposium, Nov 6-7, 1981, San Antonio, Texas Cancer Therapy and Research Center of South Texas; 1981

Monoclonal antibodies which react specifically with human breast cancer cells have been generated using hybridoma technology. Two hybridoma cell lines, H59 and H71 were established from the fusion between spleen cells immunized with ZR-75-1 cells, a cloned human breast cell line, and murine myeloma cells. H59 and H71 secrete IgMkappa antibodies which react with glandular estrogen receptor positive breast cancer cell ines, but not with more undifferentiated breast cancer cell lines. Only H71 antibody reacts with a well differentiated breast cancer cell line, T47D, which does not contain estrogen receptors. The H59 and H71 antigens have been isolated by indirect immune precipitation. H59 antigen is a p rotein complex composed of 2 peptides of approx 30,000 daltons; H71 antigen consists of 2 peptides which are about 28,000 and 2 that are 45,000 daltons. H59 antibody bound to fixed cryosections from 45 of 73 (61.6%) patients with breast cancer; H71 bound to 26 of 53 (49%). Thirty-four percent of specimens reacted with both antibodies while 28.3 percent bound neither antibody. H59 may bind a subset of estrogen receptor positive tumors, whereas H71 bound specimens which do and do not contain estrogen receptors. Both antibodies bound specimens which were progesterone receptor positive and negative. Both antibodies react with most specimens from fibrocystic disease and fibroadenomas. Since both antibodies were identified in differentiated breast cancer cell lines, and benign breast disease, the presence of the antigens in a breast cancer might indicate a more differentiated tumor and be associated with a better prognosis. (no Refs)

4. HUMAN MAMMARY EPITHELIAL ANTIGENS (HME-AGS) IN THE CIRCULATION OF BREAST CANCER PATIENTS (MEETING ABSTRACT).

Ceriani RL, Sasaki M
Bruce Lyon Memorial Research Laboratory, Children's Hospital Medical Center, Oakland, CA, 94609
4th Annual San Antonio Breast Cancer Symposium, Nov 6-7, 1981, San Antonio, Texas Cancer Therapy and Research Center of South Texas; 1981

HME-Ags are cell membrane components specific for human breast epithelial cells and are found on the cell surface of both normal and neoplastic breast epithelial cells. Heterologous antisera were prepared in rabbits against HME-Ags using defatted human milk fat globule (HMFG) as immunogen. These antisera were then used in a solid phase radioimmunoassay (RIA) to determine HME-Ag levels in the sera of breast cancer patients. High values of HME-Ags (up to 280 ng/ml of serum) were found in breast cancer with disseminated disease. Sera of normal controls, both male and female, benign breast disease and non-breast tumors showed values (below 50 ng/ml of serum) that could not be discerned from background. Further, in a recently developed 3 step immunoidentification technique (extraction, radioiodination and separation) HME-Ags were identified and characterized in the sera of breast cancer patients. In the latter case, polyacrylamide gel runs of the serum extractions demonstrated profiles corresponding to HME-Ags. Normal male and female sera as well as sera of patients with disseminated tumors other than breast did not have specific identifiable components. The conclusive identification of HME-Ags in the sera of breast cancer patients supports the results obtained by RIA and also establish that breast epithelial cell type specific antigens are released into the circulation of breast cancer patients. The optimization of the present techniques will provide cancer diagnosis with a new and useful breast tumor marker, possibly with more specificity than those al ready reported. (no Refs)

5. IMMUNOCYTOCHEMICAL STUDIES OF SECRETORY EPITHELIAL MEMBRANE ANTIGEN IN HUMAN BREAST CARCINOMAS (MEETING ABSTRACT).

Imam A, Taylor CR, Tokes ZA
Department of Biochemistry and Comprehensive Cancer Center, University of Southern California, Los Angeles, CA, 90033
4th Annual San Antonio Breast Cancer Symposium, Nov 6-7, 1981, San Antonio, Texas Cancer Therapy and Research Center of South Texas; 1981

A glycoprotein from human milk-fat-globule-membranes, which derive from mammary secretory epithelial cells, was purified to homogeneity. The purified glycoprotein was termed secretory epithelial membrane antigen (SEMA-70). Using an indirect immunoperoxidase staining method, the antigen was demonstrated on the luminal membranes of secretory epithelial cells lining the ducts of normal and neoplastic human breast tissues. Under these conditions, SEMA-70 was not detected on myoepithelial cells, fat and stromal cells, RBC, lymphocytes and cells from other glandular-epithelial tissues that included prostate, salivary, sweat and thyroid glands, colon, kidney, liver, lung, stomach, testis, and uterus. However, a weak staining of luminal membranes of collecting tubules of kidney was observed. Staining for SEMA-70 was mostly restricted to the luminal membranes of the malignant cells in well differentiated mammary carcinoma in contrast to the cytoplasmic staining observed in less well differentiated malignant cells. The extent of invasion of malignant mammary epithelial cells in axillary lymph nodes was clearly revealed by this staining technique. The results suggest that antibody to SEMA-70 is useful as a cell-type marker for the recognition of mammary epithelium, including the poorly differentiated and malignant epithelium in primary tumors and axillary lymph nodes. (no Refs)

6. MONOCLONAL ANTIBODIES THAT DEMONSTRATE SPECIFICITY FOR SEVERAL TYPES OF HUMAN LUNG CANCER.

Cuttitta F, Rosen S, Gazdar AF, Minna JD
NCI-VA Medical Oncology Branch, Div. Cancer Treatment, NCI, Washington, DC, 20422
Proc Natl Acad Sci USA; 78(7,part2):4591-4595 1981

Monoclonal antibodies with selectivity for human lung cancer were produced by immunizing BALB/c mice with an established line of human small cell lung cancer (NCI-H69) and fusing the mouse spleen cells to mouse myeloma line X63-Ag8.653. The resulting hybrid cells were initially screened by immunoautoradiography for production of antibodies that would react with NCI-H69 and another small cell lung cancer line (NCI-H128) but not its autologous B-lymphoblastoid line (NCI-H128F[illegible]). Stable monoclonal antibody-producing lines were isolated by repeated cloning. Three independently derived monoclonal antibodies, designated 525A5, 534F8, and 538F12, were found to react with three of the major types of human lung cancer (small cell, adenocarcinoma, and squamous carcinoma). They did not react with bronchioloalveolar and large cell lung cancers, myeloma, lymphomas, leukemias, osteogenic sarcoma, mesothelioma, hypernephroma, malignant melanoma, simian virus 40-transformed human fetal lung cells, skin fibroblast lines, human B-lymphoblastoid lines, human RBC, and rodent cells. Interestingly, these antibodies also bound to three out of three human neuroblastomas and two out of three breast cancers but failed to react with mouse neuroblastoma and rat pheochromocytoma. The monoclonal antibodies reacted with human small cell lung cancer tumors obtained at autopsy, but had insignificant reactions with normal human lung, liver, spleen, and skeletal muscle. We conclude that monoclonal antibodies have been generated that react with common antigenic determinants expressed on several human lung cancer types, neuroblastoma, and some breast cancers, but are not detectable by our current assays on a variety of other human tumors or normal adult human tissues. Such antibodies are of potential clinical and biological importance. (Author abstract) (50 Refs)

7. TISSUE SPECIFICITY AND CELLULAR DISTRIBUTION OF NOVIKOFF HEPATOMA ANTIGENIC PROTEINS P39, P49, AND P56.

Schmidt WN, Stryjecka-Zimmer M, Glass WF, Briggs RC, Hnilica LS
Dept. Biochemistry, Vanderbilt Univ. Sch. Medicine, Nashville, TN, 37232
J Biol Chem; 256(15):8117-8123 1981

Three Novikoff hepatoma protein antigens (approx Mr = 39,000, 49,000 and 56,000) were partially purified from Novikoff hepatoma chromatin. Rabbit antiserum to these three proteins was used to examine various rat tissues for the presence of these antigens. Immunological specificity of the antiserum was assessed using quantitative microcomplement fixation assay or by visualization of the immunoreactive complexes with peroxidase-antiperoxidase procedure after transferring the electrophoretically separated proteins to nitrocellulose sheets. The immunoreactivity was localized with the three proteins p39, p49, and p56 in Novikoff hepatoma. The p56 protein was found to be present in normal rat liver, 24-hr regenerating rat liver, fetal rat liver, or kidney, albeit in much smaller amounts as found in Novikoff hepatoma. The p49 and p39 antigens were specific for Novikoff hepatoma. Immunoabsorption experiments confirmed the specificity of this antiserum. Assessment of various subcellular fractions of Novikoff hepatoma revealed that the p39, p49, and p56 protein antigens are present in the cytoplasmic fractions as well as in isolated chromatin. (Author abstract) (34 Refs)

8. COMMON NEUROECTODERMAL ANTIGENS ON HUMAN MELANOMA, NEUROBLASTOMA, RETINOBLASTOMA, GLIOBLASTOMA AND FETAL BRAIN REVEALED BY HYBRIDOMA ANTIBODIES RAISED AGAINST MELANOMA CELLS.

Liao SK, Clarke BJ, Kwong PC, Brickenden A, Gallie BL, Dent PB
McMaster Univ., Health Sciences Centre, 1200 Main St., West, Hamilton, Ontario, L8N 3Z5, Canada
Eur J Immunol; 11(6):450-454 1981

The hybridoma system has been utilized to produce antibodies to characterize the cell surface antigens on human melanoma cells. On initial screening, two antibodies derived by the fusion of mouse myeloma cells (SP2/O-Ag14) and splenocytes from a mouse immunized with a melanoma cell line (CaCl 78-1) showed cross-reactivity with 10 melanoma cell lines and did not react with any of 4 epithelial cancer lines, or 4 normal adult fibroblast lines. However, because of reactivity with two neuroblastoma cell lines, additional testing with other neuroectodermal derivatives was carried out and revealed a broad cross-reactivity among melanomas, neuroblastomas, retinoblastomas and glioblastomas and against antigens shared by fetal but not adult brain. Thus, these results indicate the existence of common neuroectodermal antigens on melanoma cells. Before melanoma specificity can be claimed for, an antibody reactivity with nonmelanoma cells bearing these neuroectodermal antigens should be excluded. (Author abstract) (21 Refs)

9. STRUCTURAL PROPERTIES AND TISSUE DISTRIBUTION OF THE ANTIGEN RECOGNIZED BY THE MONOCLONAL ANTIBODY 653.40S TO HUMAN MELANOMA CELLS.

Natali PG, Imai K, Wilson BS, Bigotti A, Cavaliere R, Pellegrino MA, Ferrone S
(c/o Ferrone) Dept. Molecular Immunology, Scripps Clinic and Res. Foundation, La Jolla, CA, 92037
JNCI; 67(3):591-601 1981

The hybridoma 653.40S, constructed with splenocytes from an inbred BALB/c mouse immunized with cultured human melanoma cells, secreted an antibody that had been shown to recognize an antigenic determinant restricted to human melanoma cell lines. The monoclonal antibody (MoAb) 653.40S showed immunoprecipitation of two glycopolypeptides synthesized by melanoma cells, one with the apparent mol wt of 280,000 and the other one with a mol wt larger than 500,000. These two glycopolypeptides were not bridged by disulfide bonds and were peripheral rather than integral to the plasma cell membrane. Comparison of the reactivity of cells of the melanocyte lineage with the MoAb 653.40S and with the MoAb Q5/13 to human Ia-like antigens showed that the former reacted with proliferating melanocytes and melanoma cells, whereas the latter reacted only with melanoma cells. The MoAb 653.40S did not react with a large variety of surgically removed normal and tumor tissues except for some instances of basal cell and squamous cell carcinomas. These results suggested that double staining of pigmented skin lesions with the MoAb 653.40S and with an MoAb to Ia-like antigens may help to solve controversial diagnosis of melanoma. Furthermore, the MoAb 653.40S may be useful for radioimaging and immunotherapy of melanoma. (Author abstract) (32 Refs)

10. INDUCTION OF SEVERAL NEW ANTIGENS, INCLUDING A T CELL-ASSOCIATED ANTIGEN, FOLLOWING CONVERSION OF THE EBV-NEGATIVE B CELL LINE RAMOS TO EHRB-RAMOS BY EPSTEIN-BARR VIRUS.

Rosenthal KS, Shuman H, Strominger JL

Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA, 02115

J Immunol; 127(2):746-754 1981

Heteroantisera prepared against EHRB-RAMOS cells and then absorbed extensively with the syngeneic EBV-negative cell line RAMOS recognized a membrane antigen present on EHRB-RAMOS but not on RAMOS cells. The binding of the sera, anti-EHRB, was measured by several immunologic techniques that detect cell surface molecules, including cytotoxicity, immunofluorescence, and the 125I-staph protein A assay. Triton X-100 extracts of plasma membranes prepared from EHRB-RAMOS competed for the binding of anti-EHRB on EHRB-RAMOS, as measured by the staph protein A assay, whereas extracts of RAMOS membranes did not. The anti-EHRB sera also recognized the EHRA-RAMOS cell line, but binding of anti-EHRB to other EBV-converted RAMOS lines--African Burkitt lymphoma lines, newly established and well established lymphoblastoid cell lines, and EBV producer cell lines--was undetectable. The anti-EHRB sera recognized 4 T cell lines established from T cell leukemias, including CEM, HSB, YT4E, and MOLT 4. In addition, an anti-CEM serum, prepared in this laboratory, recognized the EHRB-RAMOS cells. Absorption of the serum with peripheral blood lymphocytes removed the activity of anti-EHRB to both the T cell lines and to EHRB-RAMOS, as detected by immunofluorescence using the fluorescence-activated cell sorter. The EHRB-RAMOS cells still retained B cell characteristics, since they expressed p29, 34, an antigen found on normal peripheral B cells, and did not rosette with sheep RBC. The anti-EHRB sera and anti-CEM sera were further characterized by radioimmunoprecipitation of 35S-methionine-labeled proteins of EHRB-RAMOS, RAMOS, YT4E, CEM, and HSB. Anti-EHRB recognized polypeptides of 16, 32, and 35 x 10(3) daltons on EHRB-RAMOS and 85 x 10(3) daltons on EHRB-RAMOS, CEM, HSB, and YT4E. Anti-CEM recognized polypeptides of 95 to 130 x 10(3) daltons expressed on the T cells and EHRB-RAMOS. These polypeptides were absent from or expressed to a much less extent on RAMOS. Thus conversion of RAMOS by EBV to the EHRB-RAMOS B cell line was associated with the appearance of several different antigens, some of which were also present on 4 T cell lines and on peripheral blood lymphocytes (as evidenced by absorption). (Author abstract) (42 Refs)

11. LY-M19: THE LYB-2 REGION OF MOUSE CHROMOSOME 4 CONTROLS A NEW SURFACE ALLOANTIGEN.

Tada N, Kimura S, Liu Y, Taylor BA, Hammerling Y

Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021

Immunogenetics; 13(6):539-546 1981

Spleen cells from an SJL mouse immunized with 70Z/3 cells, an established pre-B cell line, were fused with cells of the nonsecretor myeloma line NS.1. One established hybridoma cell line (clone K10.6) continuously secreted antibody that recognized a new antigenic specificity tentatively named Ly-m19. This newly found antigen is detectable on both T and B cells. Cytotoxicity assays reveal that 75% of the spleen and lymphnode cells, 35% of bone marrow cells, and 15% of thymus cells reacted with antibody of clone K10.6. Strains expressing the specificity Ly-m19.1 are characterized by negative reactions and include the strains AKR, CE/J, RF/J, GR/A, SJL, P/J, BDP/J, and LG/J. All other strains so far tested are Ly-m19.2. This strain distribution pattern distinguishes Ly-m 19 from any known murine lymphocyte alloantigen, but it parallels the Lyb-2c haplotype. Linkage test of a set of AKXL recombinant inbred strains revealed close linkage of Ly-m19 and Lyb-2 loci on mouse chromosome 4. (Author abstract) (24 Refs)

12. A MURINE STAGE-SPECIFIC EMBRYONIC ANTIGEN (SSEA-2) IS EXPRESSED ON SOME MURINE SV40-TRANSFORMED CELLS.

Shevinsky LH, Knowles BB, Howe C, Aden DP, Solter D

Wistar Inst. Anatomy and Biology, 36th St. at Spruce, Philadelphia, PA, 19104

J Immunol; 127(2):632-636 1981

A stage-specific embryonic antigen-2 (SSEA-2) found on murine preimplantation embryos is maximally expressed on 4- to 8-cell stage embryos and is present in decreasing amounts on morulae and blastocysts. This antigenic determinant is also expressed on murine teratocarcinoma cells, sperm, and some, but not all, SV40-transformed mouse cell lines. Analysis of solubilized immunoprecipitates by SDS-gel electrophoresis indicates that this cell surface molecule is not the 54,000 mol wt protein shared by teratocarcinoma and SV40-trans-formed cell lines. (Author abstract) (29 Refs)

13. PLASMA MEMBRANE ENZYMES IN BALB/C LYMPHOMAS WITH EITHER T OR B CELL PROPERTIES. I. 5'-NUCLEOTIDASE.

Zachowski A, Simonin G, Aubry J, Pommier P, Singh SN, Potter M, Paraf A

ERA 802 CNRS, Laboratoire d'Immunologie Cellulaire EPHE, Station de Recherches de Virologie et d'Immunologie, INRA, 78850 Thiverval-Grignon, France

J Receptor Res; 2(1):97-118 1981

Membrane-bound 5'-nucleotidase activity was compared in crude extracts and plasma membrane fractions from murine plasmacytomas and thymomas. Clones of the tumor cells, judged representative of different steps in B and T cell differentiation according to surface antigen markers, were derived, respectively, from Abelson virus transformed lymphomas and IgM, IgA, and IgG producing plasmacytomas, and from thymomas with surface antigen markers characteristic of T suppressor and helper cells and of early T cell differentiation. Membrane fractions were obtained through cell lysis and purification. 5'-Nucleotidase activity was characterized by the following criteria: 1) optimal pH for enzyme activity (7.5-9.5 for B type lymphocytes and 5.5-6.5 for T type cells, except in Lut 13 membranes where it was 9.5); 2) specificity of 5'-AMP as a substrate at optimal pH (for all B cell categories and Lut 13, 5'-AMP was the best substrate; for the remaining T cell types pNPP was preferred); 3) specific inhibition of 5'-nucleotidase by alpha-beta methylene ADP at optimal pH (B type cells exhibited 50% inhibition between 10 and 300 uM, whereas T type membranes required greater than 1 milliM); and 4) inhibition by EDTA at pH optimum (for B derived and Lut 13 membranes, inhibition of 5'-AMP hydrolysis occurred between 0.1 and 5 milliM EDTA, but in T type cells [illegible] inhibition was seen). 5'-Nucleotidase was found to be present on Abelson virus transformed lymphomas, plasmacytomas, and LPS stimulated blasts from nu/nu spleen, but on no thymomas except Lut 13. 5'-Nucleotidase could be a key enzyme in the purine metabolism of B cells, but not in T cells. (50 Refs)

IMMUNOLOGICAL STUDIES

14. THE GENERATION OF SPECIFIC CYTOTOXIC RESPONSES BY HUMAN LYMPHOCYTES REQUIRES ANTIGEN AND ACTIVITIES PROVIDED BY A LYMPHOKINE SUPERNATANT.

Warren HS
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Scand J Immunol; 14(1):71-76 1981

The requirements for the generation of specific cytotoxic responses by human lymphocytes have been investigated using as a model system the response to the UV light-killed mouse tumor P815. These requirements are antigen (P815UV) and activities provided by a human lymphokine (LK) supernatant. Cells that give rise to non-specific cytotoxicity can be separated on discontinuous Percoll density gradients after a 3-day incubation of peripheral blood leukocytes with the lymphokine supernatant, cells from which specific cytotoxic responses can subsequently be generated in the presence of P815UV and LK sediment at a higher density. (Author abstract) (18 Refs)

15. CHRONIC LYMPHOCYTIC LEUKEMIA OF TG-TYPE WITH NK- AND ADCC- ACTIVITY: DEMONSTRATION OF T-LYMPHOCYTIC AND MONOCYTIC ANTIGENS (MEETING ABSTRACT).

Thiel E, Stunkel K, Rieber EP, Rodt H, Thierfelder S, Feucht H, Meier CR, Goldstein G, Kung PC, Schlimok G
Institut fur Hamatologie, Munich, W. Germany
Immunobiol; 159(1/2):141 1981

Routine typing tests of a patient with a chronic lymphocytic leukemia (CLL) revealed at T-cell type of the leukemia cells (484,000 mm(3)). The cells with abundant cytoplasm containing agurophilic granules and acid phosphatase activity had strong FcIgG, but no FcIgM receptors. They exhibited both natural killing (NK) activity and antibody dependent cytotoxicity (ADCC) when tested with unsensitized or sensitized melanoma target cells. They did not suppress nor support B-lymphocyte differentiation into plasma cells and analyzed in a pokeweed mitogen (PWM)-stimulated system. Repeated analyses of the leukemia cell phenotype with monoclonal anti-WBC antibodies by quantitative fluorescence and autoradiographic methods revealed a strong reaction with the Pan-T reagents OKT3 and Lyt 3, but not with Leu-1 nor with Lyt 2 that usually stains CLL of B cell type. Completely negative were OKT 4 (specific for helper cells) and OKT 6, 9, 10 (specific for thymic phase), whereas a weak reaction of OKT 5 (specific for suppressor cells) with around 30 percent of the cells was noted. Ia-like antigens were not expressed. A very strong reaction with OKT8 (reacts with OKT4-, OKT5-subset and with suppressor cells) and with OKM 1, 2 (specific for monocytic and myelocytic cells) was measured on over 90 percent of the leukemia cells, respectively. We suggest that the hybrid cell phenotype (lympho-monocytic) which became clonally expanded in this patient may be representative for a normal cell counterpart exhibiting both NK and ADCC activity. (no Refs)

16. INTERFERON ENHANCES THE AMOUNT OF MEMBRANE-BOUND BETA2-MICROGLOBULIN AND ITS RELEASE FROM HUMAN BURKITT CELLS.

Fellous M, Bono R, Hyafil F, Gresser I
Groupe de Recherches d'Immunogenetiques de la Transplantation Humaine, INSERM U 93, Hopital Saint-Louis, 2, Place du Dr. Fournier, F75475 Paris Cedex 10, France
Eur J Immunol; 11(6):524-526 1981

Human leukocyte interferon (HuIFN-alpha) increased the amount of beta2-microglobulin on the surface of human Burkitt lymphoma cells (Ramos) and also increased the amount released into the culture medium. The effect was observed 1 hr after addition of IFN. These results suggest that the increase in beta2-microglobulin on the cell surface of IFN-treated cells is not due to a decreased shedding of antigen from the cell surface, nor an 'unmasking' of surface antigen, but rather to an increased synthesis of antigen. (Author abstract) (38 Refs)

17. EXPRESSION OF FORSSMAN ANTIGEN SYNTHESIS AND DEGRADATION IN HUMAN LUNG CANCER.

Taniguchi N, Yokosawa N, Narita M, Mitsuyama T, Makita A
Biochemistry Lab., Cancer Inst., Hokkaido Univ. Sch. Medicine, Sapporo, N15 W7, 060, Japan
JNCI; 67(3):577-583 1981

The activities of the two enzymes (UDP-acetyl-galactosamine-globoside-alpha-N acetylgalactosaminyltransferase and alpha-N-acetyl-D-galactosaminidase) involved in the synthesis and degradation of Forssman antigen were studied in uninvolved and neoplastic human lungs. The Forssman synthetic enzyme activities of 17 of 18 squamous cell carcinomas were higher than those of the uninvolved lung tissues of the subjects studied, and the degradation enzyme activities of 16 of 18 squamous cell carcinomas were higher than those of the uninvolved portions. No consistent abnormalities in both enzyme activities were seen in 28 adenocarcinomas, whereas the mean activities of the two enzymes were elevated in these neoplasms. These differences in enzyme activities between those samples may indicate that the synthesis and degradation of Forssman antigen in adenocarcinoma of the lung are expressed or repressed according to the individual, whereas in squamous cell carcinoma, these activities are expressed unrelated to the individual. (Author abstract) (20 Refs)

18. INCREASE OF T CELLS IN THE LIVER DURING HEPATOCARCINOGENESIS WITH N-2-FLUORENYLACETAMIDE IN RATS.

Okita K, Ando K, Fukumoto Y, Miyazaki M, Tsubota W, Kodama T, Takemoto T
Dept. Internal Medicine, Yamaguchi Univ. Sch. Medicine, 1144 Kogushi, Ube 755, Japan
Gan; 72(4):610-614 1981

The localization of thymus-derived lymphocytes (T cells) was investigated in rat liver by the immunofluorescence method during hepatocarcinogenesis with N-2-fluorenylacetamide. In the early stage of carcinogenesis, the number of T cells never increased significantly in livers in which hyperplastic liver nodules (population I) were seen. On the other hand, in the late stage of carcinogenesis, T cells extensively invaded hyperplastic nodules (population II) as well as hepatomas. According to the concept of cell-mediated immunity, hyperplastic nodules in the late stage might have a neoantigen(s) which evokes the response of T cells. Therefore, it may be concluded that populations I and II are biologically distinct lesions in spite of their histological identity. (Author abstract) (13 Refs)

19. AN IMMUNOLOGIC LOOK AT EARLY MOUSE DEVELOPMENT.

Edidin M
Dept. Biology, Johns Hopkins Univ., Charles and 34th St., Baltimore, MD, 21218
Cell Immunol; 62(2):247-250 1981

Studies of the surface antigens on normal mouse embryos and teratocarcinomas are summarized. The antigens might provide receptors for cell positioning in normal development, and they could also be receptors for growth-stimulating immune responses by pregnant animals. Many of these cell surface antigens appear to be glycolipids. (18 Refs)

20. IMMUNOTHERAPY OF MURINE LEUKEMIAS BY MONOCLONAL ANTIBODY. I. EFFECT OF PASSIVELY ADMINISTERED ANTIBODY ON GROWTH OF TRANSPLANTED TUMOR CELLS.

Kirch ME, Hemmerling U
Dept. Immunochemistry, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
J Immunol; 127(2):805-810 1981

The objective of the present study was to establish a model system for the evaluation of passive immunotherapy of murine leukemias. Monoclonal antibodies directed at T lymphocyte differentiation antigens (Thy 1 and Lyt 2) were tested for their effect on tumors that were grown in hosts congenic for the target antigen. Tumor challenges were selected that were at least 500 x the dose that was lethal in 50% of untreated controls. The A strain leukemia, ASL.1, was transplanted sc into A/Thy 1.1 congenic hosts. Ip administration of anti-Thy 1.2 monoclonal antibodies of the IgG3 and IgM classes reduced tumor growth. Up to 90% of the mice receiving antibody of the IgG3 subclass failed to develop tumors, whereas IgM antibodies prolonged survival time, but the mice eventually died of tumors. Antibody was most effective if administered within 24 hr of tumor inoculation; delay of antibody injection for 48 hr prolonged host survival but did not eradicate cells at the injection site or prevent metastases. The C57BL/6-derived tumors, ERLD and EL4, were evaluated for susceptibility to treatment with antibody directed at the Lyt 2.2 alloantigen using the protocol that was effective in treating ASL.1. Monoclonal antibody of the IgG2a subclass was effective in the case of C57BL/6/Lyt 2.1 congenic mice bearing ERLD, but caused a decrease in survival time of mice bearing the transplanted EL4 tumor. Thus, antibody of the appropriate immunoglobulin subclass can be effective in controlling tumor growth if administered in the optimal treatment regimen, but inherent features of the tumor cell ultimately determine whether abrogation or enhancement of growth will occur. (Author abstract) (47 Refs)

21. BIOLOGICAL ACTIVITY OF THE ANTITUMOR PROTEIN NEOCARZINOSTATIN COUPLED TO A MONOCLONAL ANTIBODY BY N-SUCCINIMIDYL 3-(2-PYRIDYLDITHIO)-PROPIONATE.

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Biochem Biophys Res Commun; 101(2):599-606 1981

The successful crosslinking of neocarzinostatin (NCS) to an IgG1 monoclonal antibody yielding hybrid proteins with biological activity is described. IgG1 is a myeloma protein obtained from the ascites fluid of pristan-treated BALB/c mice. The heterobifunctional reagent N-succinimidyl 3-(2-pyridyldithio)-propionate was used. It was shown that NCS can be linked to monoclonal antibody without loosing its biological activity as measured by the degradation of T2-DNA and bacteriostatic action. Since the hybrid protein still binds to protein A, a drastic change of antibody integrity is unlikely. The antigen binding ability of the hybrid protein, however, remains to be shown. (22 Refs)

22. REEXPRESSION OF A T/T-COMPLEX ANTIGEN (T12) IN THYMOCYTE X EMBRYONAL CARCINOMA CELL HYBRIDS.

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Somatic Cell Genet; 7(4):423-434 1981

Hybrids were constructed in which the adult thymocyte was heterozygous for the T/t complex haplotype t12 in an attempt to obtain expression of embryonic thymocyte antigens. The t haplotypes, including t12, specify mutant antigens detectable only on young embryonic cells and male germ cells but on no other adult cells. Thus the expression of t12 in +/t12 thymocyte x +/+ embryonal carcinoma cells would demonstrate the reactivation of a gene not expressed since early embryogenesis. It was also hope d that, if the t12 gene was reactivated as expected, a teratocarcinoma cell line, with robust antigen expression might be derived, that would be more suitable for serological and biochemical studies than male germ cells. The t12 gene was reactivated in the +/t12 thymocyte x +/+ embryonal carcinoma hybrids where its products were detectable both serologically and biochemically. However, the expression of the t12 antigen in the hybrids was not strong and tended to be unstable and lost with time in culture. (24 Refs)

VIRUS ASSOCIATED ANTIGENS

23. NATURAL ANTIBODIES TO THE HUMAN T CELL LYMPHOMA VIRUS IN PATIENTS WITH CUTANEOUS T CELL LYMPHOMA.

Posner LE, Robert-Guroff M, Kalyanaraman VS, Poiesz BJ, Ruscetti FW, Fossieck B, Bunn PA, Minna JD, Gallo RC
Lab. Tumor Cell Biology, NIH, Bethesda, MD, 20205
J Exp Med; 154(2):333-346 1981

Serum samples were obtained from patients with cutaneous T cell lymphoma (CTCL) and leukemia, and from 55 normal random donors. Retroviruses HTLV-CR (grown in HUT 102 cells) and HTLV-MB, isolated from patients CR and MB, respectively, were used, along with several other retroviruses. The sera were screened for the presence of natural antibody to HTLV-CR, using a solid-phase radioimmunoassay. Sera from patient CR and one other patient reacted specifically with proteins of HTLV-CR. CR serum also reacted with HTLV-MB proteins. Solid-phase immunocompetition and competition radioimmunoprecipitation assays demonstrated the specificity for HTLV-CR proteins. Patient CR antibodies were directed against viral core proteins with mol wt of 24,000 and 19,000, as shown by radioimmunoprecipitation analysis. Some reactivities to other animal retroviruses, including the baboon endogenous virus, simian sarcoma virus, feline leukemia virus, and gibbon ape leukemia virus, were demonstrated. These reactivities apparently were not virus-specific, but related to cellular antigen contamination of viral preparations or to antigens in fetal calf serum. The results indicate for the first time a specific antibody reaction to a retrovirus in humans. (38 Refs)

24. REACTIVITY OF ANTISERA TO ANTIGENS OF C-TYPE VIRUSES WITH LEUCOCYTES FROM PATIENTS WITH ACUTE LEUKAEMIA.

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Pathology; 13(2):289-298 1981

A number of previous studies have suggested that certain C-type viruses from non-human primates are associated with acute leukemia in humans. The present study sought to examine this association further by detection of antigens related to these viruses on the surface of acute leukemia cells. Antisera against the whole viruses or the major internal protein of simian sarcoma, endogenous baboon and Rauscher viruses were tested against mononuclear cells from patients with acute leukemia at various st ages of their disease in 51Cr release WBC dependent cytotoxic assays. A high proportion of the patients had antigens related to these viruses detectable on their blood WBC at some stage in their disease whereas with one exception blood WBC from non-leukemic subjects did not. The expression of these antigens did not show a close relation to the number of blast cells in blood detected on morphological grounds. Antigens related to the non-human primate viruses were detected on mononuclear cells from bone marrow samples of several non-leukemic patients which indicated they were not specifically associated with leukemia. Antigens related to the Rauscher virus were detected on cells of practically all bone marrow samples tested. These results suggest that assays to detect these antigens would be of limited usefulness to monitor disease activity in patients with acute leukemia. Their expression on blood WBC however appeared strongly associated with acute leukemia and further studies to assess the prognostic and epidemiological significance of detection of these antigens appears warranted. (Author abstract) (16 Refs)

25. CORONAVIRUS-ASSOCIATED ANTIBODIES IN NASOPHARYNGEAL CARCINOMA AND INFECTIOUS MONONUCLEOSIS.

Arnold W, Klein M, Wang JB, Schmidt WAK, Trampisch HJ
Dept. Otorhinolaryngology, Klinikum Grosshadern, Marchioninstrasse 15, D-8000 Munich 70, W. Germany
Arch Otorhinolaryngol (NY); 232(2):165-177 1981

Particles in the cytoplasm of nasopharyngeal carcinoma (NPC) cells were found which resembled coronaviruses. To determine the nature of these particles serum titer determinations were performed in NPC patients, infectious mononucleosis patients, and a control group. Epstein-Barr nuclear antigen (EBNA) test were made on tumor cells from NPC tissues and cells from cultures infected with coronaviruses. For immunological identification of coronavirus, the human coronavirus strain 229E was cultured on human fetal lung fibroblast MRC-C cells. Comparison of antibody levels showed clearly higher levels of IgG in NPC patients than in controls. IgA was the same in either group. IgM titer was in the low range in NPC patients. Infectious mononucleosis patients showed similar tiers to the NPC patients. The EBNA test was positive in all NPC cells, negative in cell cultures infected with coronavirus. In immunofluorescence tests serum from NPC patients produced intense fluorescence when applied to coronavirus-infected cells. Known high-titer coronavirus sera did not produce a similar result in MRC cells not infected with coronavirus. Evidently coronaviruses are present in the cytoplasm of NPC tumor cells. A correlation between the RNA coronavirus and the Epstein-Barr virus suggests a possible interaction between them as a factor in NPC. (35 Refs)

26. THE DETECTION OF EPSTEIN-BARR VIRUS RECEPTORS UTILIZING RADIOLABELLED VIRUS.

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J Gen Virol; 54(part1):191-195 1981

Epstein-Barr virus (EBV) was labeled with 3H-thymidine and purified about 1000-fold from the culture medium by ultracentrifugation on 5 to 30% dextran gradients. The presence of the virus was monitored by radioactivity and Epstein-Barr virus-determined nuclear antigen (EBNA) induction in sensitive indicator cells (Ramos). Peaks for both activities occurred in the 17 to 18% dextran fractions. Unlabeled virus recovered in the peak fraction was labeled with 125I. Both thymidine and 125I-labeled purified virus bound quantitatively to receptor-positive Burkitt lymphoma-derived cell lines but not to EBV-receptor-negative T-lymphocyte-derived cell lines. Thymidine-labeled virus that was allowed to bind to Raji cells was present in the interior of briefly trypsinized cells after 3 hr incubation at 37 C. The results provide a convenient method for detecting the EBV receptor by radioactively labeled virus. (Author abstract) (15 Refs)

27. HERPES SIMPLEX VIRUS AND HUMAN CANCER. II. SEARCH FOR RELATIONSHIP BETWEEN LABIAL TUMOURS AND HERPES SIMPLEX TYPE 1.

Cassai E, Rotola A, Di Luca D, Manservigi R, Meneguzzi G, Milanesi G, Califano A
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Eur J Cancer; 17(6):695-702 1981

Cellular proliferation was obtained from 30 out of 58 labial tumors examined. None of the cellular cultures obtained presented Herpes Simplex Virus type I (HSV-1) specific antigens. Tumor cell cultures demonstrated the same susceptibility to HSV-1 as cells from normal lip tissue, HEp-2 and BHK cells. The presence of HSV-1 DNA was investigated in 12 labial tumors by the blotting technique. The sensitivity of the technique made it possible to reveal 0.5 viral genome equivalent per cell. Viral DNA was not detected in any of the tumors tested. (Author abstract) (31 Refs)

28. HERPESVIRUS-INDUCED ANTIGENS IN SQUAMOUS-CELL CARCINOMA IN SITU OF THE VULVA.

Kaufman RH, Dreesman GR, Burek J, Korhonen MO, Matson DO, Melnick JL, Powell KL, Purifoy DJ, Courtney RJ, Adam E
Dept. Obstetrics and Gynecology, Baylor Coll. Medicine, Houston, TX, 77030
N Engl J Med; 305(9):483-488 1981

Tissue and serum specimens from 19 patients (24-79 yr old) with squamous-cell carcinoma (SCC) in situ of the vulva (10 patients), severe dysplasia (1), condyloma acuminatum (4), and controls seen for periodic check-up (4), were evaluated for herpes simplex virus Type 2 (HSV2) DNA-binding proteins. Nine of 10 biopsy specimens from patients with SCC or severe dysplasia reacted strongly when stained with anti-ICPS34/35 (rabbit antiserum to HSV2-infected-cell-specific protein 34/35), and eight also reacted with anti-VP143 (rabbit antiserum to nonstructural HSV2 protein); five also reacted with anti-ICSP11/12 (rabbit antiserum to HSV2-infected-cell-specific protein 11/12). All the positive reactivity observed with anti-ICSP34/35, anti-ICSP11/12 and anti-VP143 was localized in the cytoplasm rather than the nuclei, as has been previously reported in infected cells. Whole-virion structural antigens were not observed, although serological evidence of previous HSV2 infection was found in patients tested for the presence of antibodies. Serum antibodies to HSV2 were noted in nine patients with SCC, including one with mild dysplasia, and two with normal tissue. The parallel rise in the incidences of HSV2 infection and of vulvar SCC in situ and the demonstration of HSV2-specific proteins in this tissue suggest an association of HSV2 infection with this cancer. (17 Refs)

29. IMMUNOPEROXIDASE LOCALIZATION OF PAPILLOMAVIRUS ANTIGENS IN CERVICAL DYSPLASIA AND VULVAR CONDYLOMAS.

Kurman RJ, Shah KH, Lancaster WD, Jenson AB
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Am J Obstet Gynecol; 140(8):931-935 1981

Biopsies of 50 cases of cervical dysplasia (46 mild and 4 moderate) and 40 cases of vulvar condyloma acuminata (genital warts) were screened for the presence of papillomavirus antigens by means of a peroxidase-antiperoxidase method having immunospecificity against the genus-specific (common) antigen(s) of the papillomaviruses. With the use of this technique, on formalin-fixed, paraffin-embedded tissue, papillomavirus antigens were detected in cells with cytologic and histologic features of wart virus infection (so-called koilocytotic atypia). Cells showing a positive reaction for papillomavirus antigens were identified in 24 of 50 (48%) cases of cervical dysplasia and 20 of 40 (50%) cases of vulvar condyloma. The results of this study provide specific confirmation of the presence of papillomavirus antigens in cervical dysplasia and suggest that the papillomavirus may be an important factor in the etiology of this disease. (Author abstract) (18 Refs)

30. COMPARISON OF VARIOUS SEROLOGICAL AND DIRECT METHODS FOR THE DIAGNOSIS OF BLV INFECTION IN CATTLE.

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Int J Cancer; 28(2):179-184 1981

The sensitivities of several serological and direct methods for the detection of bovine leukemia virus (BLV) infection in cattle have been critically compared. Among the serological methods, the radioimmunoassay (RIA) using the BLV glycoprotein (gp) was found to be more sensitive than the RIA using the internal virion antigen (p25) and the immunodiffusion test using the virion gp antigen. The differences in sensitivity between these tests were particularly evident with sera of cattle in early stages of infection. The sensitivities of the syncytia induction assay and the competitive RIA for the direct demonstration of BLV infection in cattle are comparable. Following natural infection, antibodies to the gp antigen in most cattle were detected by the RIA several mo before infectious BLV became detectable by the SIA in the blood lymphocytes. It is concluded that the most accurate, sensitive, and rapid method for the detection of BLV infection in cattle is the RIA using the virion gp antigen. The data presented confirm that BLV infection as well as the antibody responses of naturally infected cattle to the BLV p25 and gp antigens are persistent. (Author abstract) (37 Refs)

31. CORRELATION OF BLOOD LYMPHOCYTE NUCLEAR POCKET PREVALENCE WITH ENZOOTIC BOVINE LEUKEMIA P24 VIRAL ANTIBODY TITERS.

Weber A, Bingham C, Pomeroy K
Dept. Veterinary Biology, Univ. Minnesota, St. Paul, MN, 55108
Am J Vet Res; 42(8):1395-1399 1981

The quantitative relationship between radioimmunoassay serotiters to p24 enzootic bovine leukemia viral antigen and the prevalence of lymphocytic nuclear pockets (LNP) was studied in 554 clinically normal dairy cows and bulls. Of the animals, 69% were seronegative. Of the seronegative animals, 44% had no observed LNP, whereas 93% of the seronegative animals had less than 1% LNP. However, 2.3% of the seronegative animals had substantially increased (greater than 2%) numbers of LNP, and conversely, 24% of the seropositive animals had no observed LNP. Statistical evaluation of the data, using contingency table and regression methods, provide significant (p less than 0.0001) evidence for a positive association between LNP prevalence and p24 bovine leukemia viral serotiters. Although significant, the association was weak, and hence LNP number had little value for predicting serotiter. (Author abstract) (23 Refs)

32. EVALUATION OF THE PARAMETERS OF THE ELISA PROCEDURE FOR FELINE TYPE C RETROVIRAL ANTIGENS: ASSAY OF FELV ANTIGENS IN CHRONICALLY INFECTED OR NONPRODUCER TRANSFORMED CELLS.

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Intervirology; 15(1):1-9 1981

The successful application of an improved enzyme-linked immunosorbent assay (ELISA) to the specific detection and quantitation of feline leukemia virus (FeLV) is presented. The methods described can detect FeLV antigens at the picog/ml level using a fluorometric assay for peroxidase-linked antibody. The use of a fluorogenic substrate resulted in at least a 9-fold increase in sensitivity of the peroxidase assay. FeLV antigens could be specifically detected in chronically infected cells as well as in feline sarcoma virus-transformed nonproducer mink cells which only partially express viral proteins. (Author abst ract) (26 Refs)

33. FELINE LEUKEMIA - UNIQUE AND CROSS-REACTING ANTIGENS ON INDIVIDUAL VIRUS-PRODUCING TUMORS IDENTIFIED BY COMPLEMENT-DEPENDENT ANTIBODY.

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Int J Cancer; 28(2):209-217 1981

Following exposure to feline leukemia virus (FeLV), cats that resist leukemia produce complement dependent antibodies (CDA) which lyse leukemia cells in the presence of cat complement. The CDA activity has been shown to be directed to feline oncornavirus-associated cell membrane antigen (FOCMA) found on the surface of most feline leukemias. Despite the retrovirus etiology of feline leukemia, and the ubiquity of FOCMA expression by individual tumors, we found that CDA activity did not cross-react when five feline leukemia lines were compared (FL74, F422, 3272, 3281, and 79-14940). Profiles for CDA mediated lysis of the leukemia target lines were determined for sera from 149 FeLV exposed cats, and animals were identified whose sera would selectively lyse almost any possible combination of tumors from one to five lines tested. Cross absorption and cold target inhibition studies were performed on selected sera, and a spectrum of different antigens was identified which included both individual determinants and antigens shared by some of the tumor lines. Leukemias FL74 and F422 carried a cross-reactive determinant which was distinct from a second antigen shared by 3272 and 3281; lines F422, 3272 and 3281 each also carried a unique antigen. Leukemia 79-14940 did not cross-react with other target tumor lines. Targets of CDA mediated lysis on leukemia cells may be associated with normal feline cell surface antigens, because CDA titers were sometimes reduced after serum absorption with normal cat spleen cells. The relevance of multiple FOCMA determinants is discussed in terms of tumor escape from immunity. (Author abstract) (30 Refs)

34. IN VITRO CURING OF PERSISTENT INFECTION OF HVJ (SENDAI VIRUS) CARRIER TUMOR CELLS BY SPLEEN CELLS.

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Gan; 72(4):504-511 1981

The viral antigens of hamster tumor cells persistently infected with HVJ (Sendai virus) disappeared upon transplantation, showing that HVJ persistent infection can be cured in vivo. In order to analyze these phenomena, an attempt to achieve a similar cure in vitro was made. When HVJ carrier tumor cells (GM2-HVJpi) were cultured in the presence of sera from GM2-HVJpi-tumor-bearing hamsters or rabbit antiserum against glycoproteins (GP) of HVJ, the cells showed only weak stainability with fluorescent antibody (FA). Lymphokines produced by spleen cells from GM2-HVJpi-tumor bearers could not cause GM2-HVJpi cells to lose their viral antigens. However, the viral antigens of GM2-HVJpi cells became undetectable upon cocultivation with spleen cells from either normal or GM2-HVJpi-tumor-bearing hamsters. These cells from which HVJ antigens had been lost were reconfirmed to be cured in vitro through single colony isolation and subsequent establishment of a new HVJ infection after superinfection of the isolated cells with HVJ. The above results indicate that the curing of virus persistent infection in HVJ carrier tumor cells by transplantation was due to the in vivo action of spleen cells against transplanted HVJ carrier tumor cells. (Author abstract) (17 Refs)

35. CURING OF VIRUS PERSISTENT INFECTION IN HVJ (SENDAI VIRUS) CARRIER HAMSTER TUMOR CELLS BY TRANSPLANTATION.

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Dept. Virology, Cancer Res. Inst., Kanazawa Univ., 13-1, Takara-machi, Kanazawa 920, Japan
Gan; 72(4):498-503 1981

Transplantability of hamster tumor cells in the syngeneic system was considerably reduced by HVJ (Sendai virus) persistent infection of the cells, but these HVJ carrier cells still showed tumorigenicity, especially at high transplantation doses. Therefore, the existence of HVJ antigens or infectious HVJ in the tumors formed in vivo by transplanted HVJpi (temperature-sensitive HVJ) or HVJo (non-temperature-sensitive HVJ) carrier tumor cells was examined in relation to the reduced transplantability of the cells. In stamp preparations of tumor cells, no HVJ antigens were detected from 14 days after transplantation, though they were positive if observed within 7 days. Infectious HVJ particles could also be recovered from tumor tissues which were cocultivated with LLCMK2 cells within 7 days after transplantation. However, tumor cells recultured in vitro after more than 3 wk post transplantation did not show HVJ antigens, even after various attempts at HVJ induction such as culture at low temperature, serial passages in vitro, treatment with 5-iododeoxyuridine, etc. The cytopathic effects and fluorescent antibody staining of these cells became positive when they were superinfected with wild-type HVJ, indicating a new establishment of HVJ infection after the curing of the HVJ genome initially carried. In contrast, the original HVJ carrier tumor cells were demonstrated to be completely resistant to this superinfection (one of the characteristics of persistent infection). These results seem to show that HVJ persistence in its carrier tumor cells was ultimately cured by transplantation and may provide at least a partial explanation of why the xenogenization of tumor cells by HVJ persistent infection was relatively weak. (Author abstract) (12 Refs)

36. IMMUNOSELECTION AND CHARACTERIZATION OF MOLONEY MURINE LEUKEMIA VIRUS-INFECTED CELL LINES DEFICIENT IN SURFACE GAG ANTIGEN EXPRESSION.

Edwards SA, Fan H
Peptide Biology Lab., Salk Inst., San Diego, CA, 92138
Virology; 113(1):95-108 1981

NIH/3T3 cells infected with Moloney murine leukemia virus (M-MuLV) which were deficient in gag surface antigen were selected by incubation with anti-serum to the major gag virion protein, p30, in the presence of complement. Survivors of the selection were cloned and characterized with respect to intracellular production of gag and env gene products, gag surface antigen expression as revealed by indirect immunofluorescence, and virus production. Nineteen clones tested were all positive for env gene products in cytoplasmic extracts. Seventeen of the 19 were positive for gag gene products, and 2 were negative. The gag-positive clones all produced Pr65gag (the precursor to the internal structural proteins) and they also produced gPr80gag (the precursor to the cell-surface gag antigen). The selected clones were all deficient in the presence of surface gag antigen as measured by immunofluorescent microscopy or flow microfluorimetry, and they all processed Pr65gag to mature p30 more slowly than the parental cells. In addition, all of the surface gag-deficient clones produced virus at a reduced rate. The nature of the defect in one gag-deficient clone was studied by infection of progeny virus onto uninfected NIH/3T3 cells. The resultant cells showed normal gag surface fluorescence and virus production. This suggests that the defect was cellular rather than viral. (Author abstract) (27 Refs)

37. IDENTIFICATION OF POLYPEPTIDE COMPONENTS OF ADENOVIRUS TYPE 12 TUMOR ANTIGEN FROM PRODUCTIVELY AND ABORTIVELY INFECTED CELLS AND FROM TUMOR CELLS.

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Unit. Virology, Gulbenkian Inst. Science, Apartado 14, P-2781 Oeiras Codex, Portugal
Virology; 112(2):775-779 1981

Adenovirus type 12 (Ad12) tumor antigen (T antigen) induced in productively infected KB cells, abortively infected rabbit RK13 cells, and hamster tumor cells (THA cells) was studied by immunoprecipitation and polyacrylamide gel electrophoresis. [35S]Methionine-labeled cell extracts were precipitated with anti-T serum, obtained from hamsters bearing tumors induced by Ad12, and with anti-P serum, obtained from rabbits immunized against Ad12 early proteins induced in RK13 cells. Two polypeptides with 31,000 (31K) and 19K mol wt are precipitated from all cells. Polypeptides with 16K, 15K, 13K, and 10.5K mol wt are observed in extracts from KB and THA cells only. T antigen from tumor cells also contains 57K, 50K, 45K, and 34K polypeptides. Polypeptides with 39K, 28K, and 25K mol wt are synthesized in KB and RK13 cells, mainly when the cells are pretreated with cycloheximide, but are never seen in extracts from tumor cells. Anti-P serum precipitates the 39K, 31K, 28K, 25K, and 19K polypeptides and also a 60K polypeptide from KB and RK13 cells, which probably corresponds to the DNA-binding protein. (Author abstract) (21 Refs)

38. LOSS OF FUNCTIONAL LARGE T-ANTIGEN AND FREE VIRAL GENOMES FROM CELLS TRANSFORMED IN VITRO BY POLYOMA VIRUS AFTER PASSAGE IN VIVO AS TUMOR CELLS.

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Istituto di Biologia Generale e Genetica, Univ. Naples, Naples, Italy
J Virol; 39(2):422-431 1981

We have analyzed the state, arrangement, and expression of polyoma viral DNA sequences in a number of in vitro-transformed Fischer rat cells before and after growth in vivo as tumor cells. When the in vitro lines used to induce the tumors contained only a single insert of viral sequences and did not produce either a full-size 100,000-dalton (100K) large T-antigen or free viral genomes, no differences in the above-mentioned properties were observed. By contrast, in vitro cell lines containing multiple inserts of viral sequences, a functional 100K large T-antigen, and free viral genome induced tumor cells which displayed a reduced number of inserts of viral sequences and which did not produce either a functional 100K large T-antigen or free viral genomes. All of the in vitro lines and their tumor cell derivatives expressed the polyoma virus 55K middle and 22K small T-antigen species. Possible mechanisms for the selection in vivo against cells containing a functional 100K large T-antigen and consequently free viral genomes are discussed. (Author abstract) (21 Refs)

39. SV40 GENE EXPRESSION IS MODULATED BY THE COOPERATIVE BINDING OF T ANTIGEN TO DNA.

Myers RM, Rio DC, Robbins AK, Tjian R
Dept. Biochemistry, Univ. California, Berkeley, CA, 94720
Cell; 25(2):373-384 1981

We analyzed the DNA binding properties of wild-type simian virus 40 large T antigen and found that the protein binds cooperatively to three tandem sites at a regulatory region of SV40 DNA. One consequence of this T antigen: DNA interaction is the specific repression of SV40 early RNA synthesis in vitro. We mapped a region of 85 base pairs that is necessary and sufficient to initiate early SV40 transcription in vitro. This promoter region lies directly adjacent to the third T antigen binding site but does not include the 'TATA' sequence. To determine how T antigen interacts with its binding sites to repress RNA synthesis, we analyzed transcription directed by a variety of wild-type, mutant and hybrid template DNAs. Our findings suggest that the cooperative binding of T antigen to its sites is directly responsible for inhibiting the initiation, rather than blocking elongation, of early RNA synthesis. A model is presented to explain the role of T antigen binding in the regulation of viral transcription and DNA replication during SV40 lytic infection. (Author abstract) (68 Refs)

TUMOR ASSOCIATED TRANSPLANTATION ANTIGENS

40. EVIDENCE FOR INTERACTION BETWEEN T CELL POPULATIONS OF TUMOR-BEARING AND NORMAL MICE IN IMMUNE SUPPRESSION.

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Dept. Microbiology, Thomas Jefferson Univ., 1020 Locust St., Philadelphia, PA, 19107
J Immunol; 127(3):1236-1240 1981

Spleen cells of DBA/2 mice bearing sc implants of the syngeneic tumor L5178Y induce suppression of the in vitro antibody response of normal spleen cells to sheep RBC (SRBC). Cells mediating suppression are detected in the spleens of tumor-bearing mice as early as 24 hr post-implantation but are no longer detected there 15 days post-implantation. These spleen cells are nylon wool nonadherent, sensitive to anti-Thy 1.2 + C and anti-Lyt 1.1 + C, and insensitive to anti-Lyt 2.1 + C treatment. The anti-SRBC response of the unfractionated spleen cells from the tumor-bearing mice is not itself suppressed at the cell numbers used. This along with the finding that suppression occurs in the presence of spleen cells from normal mice suggest that a cell population from the normal mouse spleen is also involved in the suppression. Spleen cells from mice inoculated with irradiated (nonproliferating) L5178Y cells are similarly capable of mediating nonspecific suppression for the same limited period of time after the inoculation. In addition, spleen cells from mice stimulated with several nontumorigenic cellular antigens interact with normal spleen cells to produce suppression. These findings suggest that suppression observed in vitro with spleen cells from these tumor-bearing mice may be the result of antigen-activated cells triggering normal immunoregulatory cells. (Author abstract) (30 Refs)

41. MIXED LYMPHOCYTE REACTIVITY IN SPLEEN CELLS FROM F-9 TUMOR-BEARING MICE. I. SUPPRESSOR CELL INDUCTION AND CHARACTERIZATION.

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Immunology Branch, Building 10, Room 4B-17, NCI, NIH, Bethesda, MD, 20205
Cell Immunol; 62(2):334-340 1981

The immune capacity of spleen cells from F-9 tumor-bearing mice was assessed in a one-way mixed leukocyte culture (MLR) and in MLR mixing experiments. Alloreactivity was found to be significantly depressed in mice bearing palpable tumors. Mixing experiments demonstrated that the reduced alloreactivity was due to suppressor cell activity in the spleens of the tumorous mice. Suppressor cells were characterized as adherent, Ly2+ T cells. This study provides the basis for an analysis of the cell surface antigens on F-9 embryonal carcinoma cells which lead to the induction of suppressor T cells in these mice. (Author abstract) (22 Refs)

42. MIXED LYMPHOCYTE REACTIVITY IN SPLEEN CELLS FROM F-9 TUMOR-BEARING MICE. II. FUNCTIONAL CROSS-REACTIVITY BETWEEN F-9 CELLS AND TESTICULAR CELLS.

Hurtenbach U, Bennett D, Bluestone JA
Immunology Branch, NCI, NIH, Building 10, Room 4B-17, Bethesda, MD, 20205
Cell Immunol; 62(2):341-349 1981

Previous serological analysis has revealed cross-reactive antigens on F-9 cells and mouse germ cells. Therefore, we investigated whether suppressor activity in spleen cells from F-9 tumor-bearing mice can be restimulated in vitro by adding F-9 cells or testicular cells to mixed lymphocyte cultures. We found equal potentiation of suppressor T-cell activity with F-9 cells and with syngeneic testicular cells, as shown by sensitivity to anti-Lyt 2.2 plus complement treatment. Suppressor activity of spleen cells from other tumor systems tested was not enhanced. The data suggest that the same or cross-reactive antigens on F-9 teratocarcinoma cells and testicular cells may have similar regulatory functions. (Author abstract) (19 Refs)

43. THE REQUIREMENT OF IA-POSITIVE ACCESSORY CELLS FOR THE INDUCTION OF TUMOR-SPECIFIC CYTOTOXIC T LYMPHOCYTES IN VITRO.

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Dept. Immunology, Univ. Occupational and Environmental Health, Sch. Medicine, 1-1 Iseigoaka, Yahatanishiku, Kitakyushu 807, Japan
Cell Immunol; 62(2):425-435 1981

The mechanism for the induction of cytotoxic T cells specific for tumor-associated antigens was studied by using fractionated responder T cells, tumor cells, and accessory cells in vitro. The tumor-specific cytotoxic T cells were induced by culturing immunized spleen cells with the tumor cells in vitro for 5 days. Nylon-column-purified T cells alone did not induce cytotoxic T cells upon culture with tumor cells, but the addition of normal spleen cells as accessory cells did successfully induce the cytotoxic T cells, suggesting that the presence of accessory cells is required for the activation of tumor-specific cytotoxic T cells in vitro. The accessory function was associated with spleen cell populations adhering to a plastic dish, a Sephadex G-10 column or a nylon wool column, and was sensitive to anti-Ia serum and C treatment, but was resistant to anti-Ig serum or anti-Thy 1 serum and C treatment, suggesting that the accessory cells are Ia-positive macrophages. Not only syngeneic but also allogeneic macrophages had the accessory function and the allogeneic macrophages were also Ia positive. These results suggest that Ia-positive macrophages play a crucial role in the induction of tumor-specific cytotoxic T cells in vitro. The possible role of Ia-positive accessory cells in the induction of tumor-specific cytotoxic T cells is discussed from the standpoint of cellular interactions. (Author abstract) (32 Refs)

44. IMMUNE RESPONSIVENESS OF HRS/J MICE TO SYNGENEIC LYMPHOMA CELLS.

Johnson DA, Meier H
Jackson Lab., Bar Harbor, ME, 04609
J Immunol; 127(2):461-464 1981

HRS/J, hr/hr and hr/+ mice were evaluated and their ability to resist challenge with a syngeneic tumor, HTU, and for their ability to mount a protective immune response when immunized in vivo with inactivated HTU cells previous to challenge with viable tumors. The heterozygous (hr/+) mice responded more strongly than the homozygous (hr/hr) mice. This response was characterized by the presence of an enhanced ability of spleen cells from immunized mice to form blasts in vitro when incubated with purified murine leukemia viruses (MuLV). We conclude that the in vivo response of HRS/J mice against this tumor is directed, in part, against MuLV antigens expressed on the tumor cells and that the relatively weak response of hr/hr spleen cells to these antigens may be mechanistically linked to their tumor susceptibility. (Author abstract) (17 Refs)

45. ESCAPE OF METASTASIZING CLONAL TUMOR CELL VARIANTS FROM TUMOR-SPECIFIC CYTOLYTIC T LYMPHOCYTES.

Bosslet K, Schirrmacher V
Institut fur Immunologie und Genetik, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, 6900 Heidelberg, W. Germany
J Exp Med; 154(2):557-562 1981

The spontaneous, highly metastatic ESb tumor variant arose from the chemically-induced DBA/2 lymphoma L5178Y (Eb) tumor. It is characterized by a tumor-associated transplantation antigen (TATA). This antigen is recognized by syngeneic secondary antitumor cytolytic T lymphocytes (CTL). During metastasis of twice-cloned cell lines of this tumor, immunoresistant variants develop that are not susceptible to lysis by CTL. These variants are detected in the spleens of normal syngeneic mice. Experimental evidence indicates that ESb TATA is reduced or non-existent in the variants. They apparently did not have a differentiated TATA. The variants remained stable in over 100 tissue culture generations. They were shown not to be preexisting in the original tumor cell population. The high frequency with which these variants occur is suggested as a cause of the ineffectiveness of specific immunization against the ESb tumor type. (15 Refs)

46. SOME MURINE ALLOGENEIC ORGAN AND TUMOR GRAFTS WHICH ARE NOT REJECTED: THE IMPORTANCE OF LOCAL FACTORS.

Russell PS

Dept. Surgery, Harvard Medical Sch., Massachussetts General Hosp., Boston, MA, 02114

Cell Immunol; 62(2):287-292 1981

Survival of grafts was studied in mice. Donors were from the B10.D2 strain, and recipients were from the B6AF1 strain. In one study kidneys were transplanted with primary vascular union. About 70% of the transplanted kidneys continued to function for many wk, which is striking since skin grafts between these strains are regularly rejected. Histological examination of the transplanted kidneys showed moderate rejection reaction in the first wk or two. This reaction was greatly reduced after about 1 mo. Donor-strain skin grafts placed on kidney transplant recipients generally survived. Renal tissue implanted im was rejected. A few B6AF1 mice parabiosed to syngeneic mice bearing B10.D2 kidneys accepted transplants of B10.D2 hearts, indicating the presence of a transferable factor causing nonreactivity. When B10.D2 sarcomas were transferred to B6AF1 mice which had previously rejected B10.D2 skin grafts, no tumor growth was noted. This indicated that the tumor cells shared some of the same antigens as the skin grafts. Donor-strain tumors caused subsequent skin grafts to be rejected. An effective cure for donor-strain tumors was found by injecting 2.0 mg cyclophosphamide, followed in 2 days by ip injection of donor-strain lymphoid cells. The results indicate that transplant survival is affected by local factors, and that in the kidney, the mode of attachment is critical. (12 Refs)

CLINICAL DIAGNOSTIC STUDIES

47. CYTOCHEMISTRY AND MEMBRANE MARKERS IN ACUTE LYMPHATIC LEUKAEMIA (ALL).

Huhn D, Thiel E, Rodt H, Andreewa P

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Scand J Haematol; 26(4):311-320 1981

One hundred thirty-six patients suffering from ALL were subdivided into 5 subtypes (C-ALL, C/T-ALL, pre-T-ALL, B-ALL) according to rosetting tests and using specific antisera directed against membrane antigens. In addition, leukemic blasts of all patients were investigated according to morphological and cytochemical criteria. In APh and ANAE, indices and the percentages of cases showing a granular staining pattern were high in pre-T- and in T-ALL, but low in C/T- and in C-ALL. PAS-staining, conversely, was more pronounced in C/T- and C-ALL. APh proved to be more discriminative for recognition of the T- and Pre-T-ALL subgroups than ANAE, but ANAE-cytochemistry may be useful to detect contaminating normal T-lymphocytes in ALL. Receptors for C3 were more frequent in C- and in T-ALL than in C/T- and in pre-T-ALL, receptors for Fc were distributed equally among all subtypes. Positivity of C3-and Fc-receptors was not correlated with cytochemical results. Morphological criteria were not sufficient for subclassification of ALL; the combination of APh- and PAS-staining, however, is valuable to differentiate between C-subgroups and T-subgroups. (Author abstract) (36 Refs)

48. CHRONIC MYELOMONOCYTIC LEUKEMIA. IN VITRO BEHAVIOR OF A CLEAR-CUT ENTITY.

Burgaleta C

Servicio de Hematologia-Hemoterapia, Centro Especial 'Ramon y Cajal', Madrid-34, Spain

Sangre (Barc); 26(3):276-282 1981

The cell proliferation and maturation patterns of chronic myelomonocytic leukemia (CMML) were studied by means of liquid- and semisolid-medium cultures of bone marrow and peripheral blood cells from these patients. Bone marrow cell proliferation was normal in both media and a normal number of colonies (CFU-C) was obtained on agar. The maturation was equally good, with less than 10% juvenile forms after 7 days of culture. The proliferation and the number of colonies obtained from peripheral blood were normal as well, the transformation into macrophages in liquid medium being delayed. When assessing the functional activity of monocytes it was found that such cells had the capability to release colony-stimulating substances (CSA), and chemotactic ability; their phagocytic power for Candida was decreased, although the fungicidal capability was preserved. According to these results, a) CMML can be differentiated from other forms of preleukemia, and b) the alterations in this entity seem to rest on the proliferation of abnormal myelocytes or myelomonocytes, whose consequence would be the presence of peripheral monocytosis with cells of a lesser maturity and functional capabilities than normal. (Author abstract) (31 Refs) (In SPA)

49. SERUM EPSTEIN-BARR ANTIBODY LEVELS IN ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN.

Holy J, Hrodek O, Hynieova H, Petrtylova K, Srajer J, Vanecek K
Ustav vyzkumu vyvoje ditete, Fakulta detskeho lekarstvi KU, Dostalova 12, 162 00 Praque 6, Czechoslovakia
Cesk Pediatr; 36(5):248-253 1981

The serum levels of Epstein-Barr virus capsid antigen antibody were determined by the indirect immunofluorescence test in 21 children (4 boys and 7 girls, 21-140 mo old) before and after the beginning of treatment. The antibody levels were 289.8 (versus 349.5 in the controls) before treatment and 165.3 after treatment (p less than 0.05). The decrease was from 226.3 to 97.5 in the boys (p 0.01), but there was no decrease in the antibody levels in the girls (475.5 before and after treatment, versus 208.6-280.7 in the controls). A direct immunosuppressive effect of the treatment is suggested as one of the possible causes of the decrease in the antibody level. (22 Refs) (In CZE)

50. RESPONSE OF CUTANEOUS T CELL LYMPHOMA TO THERAPY WITH HYBRIDOMA MONOCLONAL ANTIBODY.

Miller RA, Levy R
Div. Oncology, Stanford Univ. Medical Center, Stanford, CA, 94305
Lancet; 2(8240):226-230 1981

A murine hybridoma monoclonal anti-T-cell antibody was given to a patient with advanced cutaneous T cell lymphoma. The patient tolerated 17 treatment courses over 10 wk without symptoms of toxicity. Each treatment caused a reduction in circulating T cells which reached a stable level after 2 wk of therapy. Antigenic modulation was observed after each treatment but was fully reversed within 3 to 4 days; therefore the treatment was given twice weekly. Monoclonal antibody produced a striking clinical response in skin, lymph nodes, and blood but complete remission was not achieved. Since the remaining disease was antigen postive, failure to eradicate all tumor cells was not a result of immunoselection. At no time did the patient show an antimouse immune response. (Author abstract) (11 Refs)

51. DIFFERENTIATION OF MEDULLOBLASTOMA. STUDIES INCLUDING IMMUNOHISTOCHEMICAL LOCALIZATION OF GLIAL FIBRILLARY ACIDIC PROTEIN.

Palmer JO, Kasselberg AG, Netsky MG
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J Neurosurg; 55(2):161-169 1981

A series of medulloblastomas was studied by light microscopy. The tumors were variable; astrocytic, ependymal, neuronal, and probable oligodendroglial differentiation was present. Features of glioblastoma multiforme occurred in one case. Immunoperoxidase staining for glial fibrillary acidic protein (GFAP), an antigen found only in astrocytes and ependymal cells, revealed astrocytic differentiation in 11 of 13 cases. The two GFAP-negative tumors were histologically undifferentiated. A new classification of medulloblastomas is presented, based on the multiple types of differentiation of these tumors. Neuronal, astrocytic, ependymal, and small-cell types are described. Undifferentiated tumors were more frequent in younger children. The differentiation of medulloblastoma is correlated with recent experimental studies of gliogenesis and neurogenesis. A hypothesis that medulloblastoma is a stem-cell neoplasm is presented, based on these comparative data. (Author abstract) (43 Refs)

52. DIAGNOSIS, STAGE AND PROGNOSIS OF BREAST CANCER BY ASSAY OF BREAST CANCER-ASSOCIATED ANTIGEN-SENSITIZED T CELLS: DETECTION OF PRIMARY AND RECURRENT DISEASE (MEETING ABSTRACT).

Ramey WG
St. Luke's Roosevelt Hospital Center, New York, NY, 10025
4th Annual San Antonio Breast Cancer Symposium, Nov 6-7, 1981, San Antonio, Texas Cancer Therapy and Research Center of South Texas; 1981

Peripheral blood lymphocytes (PBL) from 267 patients with breast disease were assayed for the detection of T cells sensitized to soluble breast tumor-associated antigen (BTA) extracts by the antigen-stimulated active rosette-forming T cell (AgARFC) assay. Sensitization to BTA by T cells from PBL, detected by significant increases in rosette formation with sheep RBC at 37 C in the presence of BTA, was correlated with pathological diagnois, stage of disease, and survival (up to five yr followup). Primary breast cancer was detected preoperatively in 96% of stage I, 76% of stage II, 57% of stage III, and 68% of stage IV patients (p less than 0.01). Only 6% of patients with fibroadenomas but 28% of patients with fibrocystic disease (FCD) had false positive assays; one of these FCD patients has recently developed breast carcinoma. Sixty-four percent of patients with local or systemic tumor recurrence after prior mastectomy were reactive to BTA at entry into this study, and the degree of reactivity correlated with subsequent survival (r equal + 0.78, p greater than 0.01). Serial assay of 31 patients after mastectomy showed that 78% of patients with positive AgARFC assays 2 or more mo postoperatively have had tumor recurrence, compared to only 6% of patients with negative assays after mastectomy (p less than 0.01). In the past yr, the rapidity and reproducibility of the AgARFC assay have been enhanced by the development of a microcomputer-controlled automated counting technique. This study suggests that, using this new technology, sensitive and cost-effective detection of early primary or recurrent breast carcinoma by noninvasive means will be feasible. (no Refs)

53. INCREASED DETECTION OF MAMMARY CARCINOMA CELLS IN MARROW SMEARS USING ANTISERA TO EPITHELIAL MEMBRANE ANTIGEN.

Dearnaley DP, Sloane JP, Ormerod MG, Steele K, Coombes RC, Clink HMcD, Powles TJ, Ford HT, Gazet J-C, Neville AM
Ludwig Inst. Cancer Res., Royal Marsden Hosp., Sutton, Surrey SM2 5PX, England
Br J Cancer; 44(1):85-90 1981

We have developed a technique for the immunocytochemical staining of marrow smears using antiserum to epithelial membrane antigen (EMA). This membrane component is confined to, but widely distributed in, epithelial tissues and tumors derived from them, and is strongly expressed by infiltrating breast carcinoma cells. Marrow aspirates from patients with both early and metastastic breast cancer have been examined, and the results of immunocytochemical staining compared with conventional cytology and histology. Staining with antiserum to EMA enabled us to detect small numbers of carcinoma cells, and increased the yield of positive samples. Furthermore, using this technique, we found malignant cells in the marrow of patients with primary breast cancer with no other evidence of metastastic disease. Thus immunocytochemical staining for EMA may be of value in the detection of micrometastases in patients with primary breast carcinoma. (Author abstract) (13 Refs)

54. THE CLINICAL COURSE IN PATIENTS WITH RENAL CARCINOMA SUBJECTED TO EXTRACORPOREAL IMMUNOADSORPTION.

Wolf H, Langvad E, Hyden H
Dept. Urology, Hvidovre Univ. Hosp., 2560 Hvidovre, Denmark
Br J Urol; 53(2):89-94 1981

The clinical course in four patients with renal carcinoma stages II, III or IV subjected to periods of extracorporeal immunoadsorption is reported. By this technique we have previously demonstrated that it is possible to isolate and remove circulating tumor associated antigens from the blood stream. The removal of these antigens should, according to present-day concepts, make it possible to control 'antigenic inhibition' and/or 'blocking', thus facilitating the immune mediated destruction of residual tumor cells in advanced disease. The clinical course in these patients, however, did not differ from the expected clinical course in other such patients. The failure of extracorporeal immunoadsorption to alter the natural course of the disease may be due either to too large a tumor burden or to the possibility that spontaneous tumors during evolution and progression become independent of immune restriction. (Author abstract) (12 Refs)

55. DETECTION OF ABH TISSUE ISOANTIGENS BY IMMUNOPEROXIDASE METHODS IN NORMAL AND NEOPLASTIC UROTHELIUM. COMPARISON WITH THE ERYTHROCYTE ADHERENCE METHOD.

Coon JS, Weinstein RS
Dept. Pathology, Rush-Presbyterian-St. Luke's Medical Center, 1753 West Congress Parkway, Chicago, IL, 60612
Am J Clin Pathol; 76(2):163-171 1981

The expression of the ABH blood group antigens (BGAg) by carcinomas of the urinary bladder at the time of initial biopsy heralds a relatively benign clinical course, whereas antigen deletion in histologically similar tumors is often predictive of tumor recurrences and invasion. The use of BGAg as a tumor marker in the clinical setting has been limited by difficulties in demonstrating BGAg in tissue sections with the erythrocyte adherence test, especially for antigen H. In this study, immunoperoxidase methods were used to detect BGAg in deparaffinized tissue sections of normal and malignant human urothelium, and the results were compared with those of the erythrocyte adherence test performed on adjacent sections. Results with the two methods were similar for antigens A and B; however, a novel lectin-antilectin immunoperoxidase method was clearly superior for detecting antigen H. The immunoperoxidase method significantly reduced false-positive test results for antigen deletion in normal urothelium and more accurately predicted the subsequent clinical course in patients having urinary bladder cancer. (Author abstract) (32 Refs)

56. SPECIFIC RED CELL ADHERENCE: IMMUNOLOGIC EVALUATION OF RANDOM MUCOSAL BIOPSIES IN CARCINOMA OF THE BLADDER.

Stein BS, Reyes JM, Petersen RO, McNellis D, Kendall AR, Soloway MS
Dept. Urology, Temple Univ. Health Science Center, Philadelphia, PA
J Urol; 126(1):37-40 1981

We studied 103 random biopsies from patients with overt transitional cell carcinoma of the bladder for specific red cell adherence. We evaluated 62 random biopsies from patients whose primary tumors were positive for specific red cell adherence and 100% of the biopsies in these patients also were positive for specific red cell adherence regardless of the pathologic finding in the random biopsy. We evaluated 41 random biopsies from patients whose primary bladder tumors were negative for specific red cell adherence and only 27% of all biopsies in this group of patients were positive for specific red cell adherence. Thus, we found that in 92 of the 103 random biopsies (89%) the specific red cell adherence of the biopsy agreed with that of the primary tumor. The loss of red cell antigens in random biopsies that are histologically normal may prove to be the earliest measurable changes of the malignant potential of the urothelium. (Author abstract) (24 Refs)

57. PRACTICAL UTILITY OF SPECIFIC RED CELL ADHERENCE TEST IN BLADDER CANCER.

Catalona WJ
Jewish Hosp. St. Louis, 4960 Audubon Ave., St. Louis, MO, 63110
Urology; 18(2):113-117 1981

There is a highly significant correlation between specific red cell adherence (SRCA) tests for ABO(H) blood group antigens and the biologic potential of a bladder cancer in terms of both superficial tumor recurrences and the subsequent development of invasive cancer. The correlation with superficial recurrences is of limited practical value because almost one half of patients with antigen-positive tumors have superficial recurrences. Similarly, because in approx one third of patients with SRCA-negative tumors invasive cancer does not develop, SRCA tests cannot be used to select patients for early cystectomy. Because invasive cancer proceeds to develop in less than 10% of patients with high-grade, antigen-positive tumors, SRCA tests may be of use to identify patients with high-grade tumors who deserve a trial of conservative therapy. SRCA tests must be interpreted with caution in patients who have been treated previously with radiation therapy or thiotepa, in whom false positive tests may occur, and in patients with type O blood in whom false negative tests may occur. (Author abstract) (11 Refs)

58. PROSTATIC-SPECIFIC ANTIGEN: AN IMMUNOHISTOLOGIC MARKER FOR PROSTATIC NEOPLASMS.

Nadji M, Tabei SZ, Castro A, Chu TM, Murphy GP, Wang MC, Morales AR
Dept. Pathology (R-1), Univ. Miami, P.O. Box 016960, Miami, FL, 33101
Cancer; 48(5):1229-1232 1981

Antiserum to a human prostate-specific antigen was raised in a rabbit and utilized by immunoperoxidase staining to evaluate its potential value as a diagnostic histologic marker for tumors of prostatic origin. All primary and metastatic prostatic malignancies reacted positively, whereas nonprostatic neoplasms did not stain with this procedure. This is the first immunohistochemical marker for prostate gland epithelium which does not represent prostatic acid phosphatase. (Author abstract) (8 Refs)

59. PROSTAGLANDIN E2 AFFECTS THE TUMOR IMMUNE RESPONSE IN PROSTATIC CARCINOMA.

Kaneti J, Thomson DM, Reid EC, Catalona WJ
(c/o Thomson), Montreal General Hosp., 1650 Cedar Ave., Montreal, Quebec H3G 1A4, Canada
J Urol; 126(1):65-70 1981

Antitumor immunity to prostatic carcinoma (PC) was assayed by the tube WBC adherence inhibition (LAI) assay. Peripheral blood WBC (PBL) from 37 patients with PC and 128 patients without PC were incubated separately with extracts from PC and from an unrelated control cancer, and the non-adherence index was calculated. The number of patients with PC who had a positive response (non-adherence index greater or equal to 30) was small. Nevertheless, the mean non-adherence index (11) of the patients with PC was statistically different (p less than 0.02) from the mean non-adherence index (2) of the subjects without PC . Of patients with PC 14% (5 of 37) had positive LAI responses, compared to 1.5% of control subjects (2 of 128) (p less than 0.05). Sixty patients diagnosed clinically as having benign prostatic hyperplasia were screened by the LAI test and the nonadherence index results then were evaluated with the histopathological diagnosis of the surgical specimen. Of the patients with benign prostatic hyperplasia three (5%) had Stage A PC, and one of these three patients (33%) had a positive LAI test. After in vitro treatment of the PBL with 10(-6) M prostaglandin E2 11 of 18 patients with PC (61%) and 1 of 35 subjects without PC (3%) had positive LAI responses. The ability of prostaglandin E2 to heighten the LAI response of the PBL from patients with PC suggests that there is a functional defect in the antitumor response of the PBL, possibly caused in part by an excess of circulating tumor antigen. In fact, this is supported by the high mean non-adherence index (19) in patients with PC who had serum prostatic acid phosphatase within normal limits, while patients with an elevated prostatic acid phosphatase had a low mean non-adherence index (0.2). Therefore, patients with PC are expressing an antitumor response to PC but this response is weak even when the clinical stage of the disease seems to be early. (Author abstract) (25 Refs)

60. FACTOR VIII IN KAPOSI'S SARCOMA.

Guarda LG, Silva EG, Ordonez NG, Smith JL
(c/o Ordonez) Dept. Pathology, M. D. Anderson Hosp. and Tumor Inst., Texas Medical Center, Houston, TX, 77030
Am J Clin Pathol; 76(2):197-200 1981

The immunoperoxidase technic was applied to 15 skin lesions of Kaposi's sarcoma to localize factor VIII-related antigen. Factor VIII-related antigen serves as a tissue-specific marker for endothelial cells. Positive staining was observed in all cases. These findings support the endothelial origin of the lesion of Kaposi's sarcoma. (Author abstract) (18 Refs)

OTHER RELATED STUDIES

61. IMMUNOLOGIC ASPECTS OF CANCER.

Oettgen HF
Clinical Immunology Service, Memorial Sloan-Kettering Cancer Center, New York, NY
Hosp Pract; 16(7):85-88,90,93-95 1981

Current research in the field of tumor immunology is reviewed with special emphasis on the identification of tumor-specific antigens. In vitro techniques demonstrated that tumors and leukemias induced by oncornaviruses express the transplantation antigens. Tumors induced by chemical antigens or oncogenic viruses were found to vary in their ability to render mice immune to subsequent challenge with the same tumor. Human tumor-specific antigens defined by heterologous sera were shown to be differentiation antigens. An autologous typing of greater than 200 melanoma patients revealed three classes of surface antigens, ie antigens restricted to the autologous tumor and not detectable on autologous normal cells; shared tumor ant igens, expressed by autologous as well as by some allogeneic tumors of similar or different origin; and antigens widely distributed on autologous, allogeneic, and xenogeneic normal and malignant cells. Development of serologic typing systems for defining cell surface antigens of melanoma and other cancers provided the basis for assaying a number of different melanoma vaccines. (5 Refs)

62. ABSENCE OF COMMON ALL ANTIGEN ON NORMAL BIPOTENT MYELOID, ERYTHROID, AND GRANULOCYTE PROGENITORS.

Clavell LA, Lipton JM, Bast RC, Kudisch M, Pesando J, Schlossman SF, Ritz J
Instituto Hematologico Oncologico Pediatrico, Hospital Universitario de Ninos, Recinto de Ciencias Medicas, G.P.O. Box 5067, San Juan, PR, 00936
Blood; 58(2):333-336 1981

The presence of the common acute lymphoblastic leukemia antigen (CALLA) on leukemic cells from the great majority of patients with non-T-cell acute lymphoblastic leukemia and chronic myelogenous leukemia in blast crisis suggests that CALLA could be a differentiation antigen expressed by normal lymphoid and myeloid stem cells. Treatment with a murine monoclonal anti-CALLA antibody and complement lysed CALLA-positive leukemic cells quantitatively, whereas similar treatment of nucleated cells from peripheral blood and bone marrow failed to affect the expression, in semisolid culture, of CFU-G/E, BFU-E, CFU-E, or CFU-C. These data suggest that CALLA is not a normal differentiation antigen of the myeloid bipotent cell or its committed progenitors. (Author abstract) (20 Refs)

63. ULTRASTRUCTURAL STUDY OF MEMBRANE GLYCOCALYX IN PRIMARY AND METASTATIC HUMAN AND RAT MAMMARY CARCINOMA.

Ghosh L, Nassauer J, Faiferman I, Ghosh BC
NCI, 7910 Woodmont Ave., Rm. 4804, Bethesda, MD, 20205
J Surg Oncol; 17(4):395-401 1981

The glycocalyx of primary and metastatic tumors was compared by ruthenium red staining and electron microscopy. Two systems were studied: human primary and metastatic breast tumors and rat primary and metastatic mammary carcinomas. A considerable diminution in the amount of glycocalyx was detected in both systems when primary tumors were compared with metastases. These results are consistent with observations of others showing that metastatic tumors shed glycoprotein antigens to the circulation; this may provide an immune escape mechanism for tumor cells, allowing their dissemination. (Author abstract) (16 Refs)

64. EPSTEIN-BARR VIRUS CO-RECONSTITUTED WITH SENDAI VIRUS ENVELOPES INFECTS EPSTEIN-BARR VIRUS-RECEPTOR NEGATIVE CELLS.

Shapiro IM, Klein G, Volsky DJ
Dept. Tumor Biology, Karolinska Institutet, Box 60400, S-104 01 Stockholm, Sweden
Biochim Biophys Acta; 676(1):19-24 1981

Epstein-Barr virus (EBV) was co-reconstituted with Sendai virus envelopes. The reconstituted 'hybrid' virus could bind and penetrate into EBV-receptor negative cells. Using this approach, T-cell-derived human and mouse leukemia cells, human T-lymphocytes and mouse spleen cells were successfully infected as judged by the induction of EBV-determined antigens and stimulation of DNA synthesis. The T-cell-derived human leukemia line Molt-4, that can absorb EBV but without virus penetration, could be also infected by the reconstituted EBV. (Author abstract) (27 Refs)

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IMMUNOBIOLOGY AND CANCER

Tumor-Associated Antigens

SERIES CB05 No. 82/02

FEBRUARY, 1982

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DETECTION/ CHARACTERIZATION/ ISOLATION

1. CHARACTERIZATION OF A RABBIT ANTI-HUMAN MALIGNANT GLIOMA ANTISERUM.

Schnegg JF, De Tribolet N, Diserens AC, Martin-Achard A, Carrel S
Neurosurgical Service, CHUV, 1011 Lausanne, Switzerland
Int J Cancer; 28(3):265-269 1981

An antiglioma antiserum was produced by immunization of a rabbit with membrane-enriched preparations of a human malignant glioma cell line, LN-18. After extensive absorption, this antiserum reacted exclusively with antigenic determinants present on 7 out of 16 malignant glioma cell lines tested, as shown by complement-dependent cytotoxicity in a 51Cr-release assay. This glioma specificity could be further confirmed by quantitative absorption experiments where cells from a glioma line, Ln-135, abolished the cytolytic reactivity of the antiserum against four other glioma lines. The stepwise absorp tion of the crude antiserum consisted of: Step 1, absorption with normal peripheral blood lymphocytes from 10 individual donors; Step 2, absorption with a pool of cells from four different lymphoblastoid cell lines and one endometrial carcinoma; Step 3, absorp-

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tion with cells from a colon carcinoma; and Step 4, absorption with cells from two different melanoma lines. After each absorption step the antiserum was tested by complement-dependent cytotoxicity against a large panel of malignant glioma lines and control non-glioma cell lines. After the absorptions from Steps 1 and 2 the antiserum reacted with all cell lines tested, while after Step 3 absorption, it reacted only with cells from malignant glioma, melanomas and fetal brain. Quantitative absorption experiments performed at this stage with fetal brain cells showed that the reactivity for fetal brain and melanoma cells could be abolished, while the antiserum was still cytolytic for malignant gliomas. After the absorption from Step 4, the antiserum reacted exclusively with seven malignant gliomas. After a further absorption with normal adult brain homogenate, the antiserum still reacted with four of the seven malignant glioma cell lines. Thus, the antiserum described here recognized three types of antigens: antigens common to cells of neuroectodermal origin, antigens shared by malignant gliomas and adult brain, and antigens expressed only on some gliomas. (Author abstract) (22 Refs)

2. A MONOCLONAL ANTIBODY DETECTING AN ANTIGEN SHARED BY NEURAL AND GRANULOCYTIC CELLS.

Kemshead JT, Bicknell D, Greaves MF
Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London, England
Pediatr Res; 15(9):1282-1286 1981

A monoclonal antibody, MI/N1, is described that reacts predominantly with fresh neuroblastoma tissue, human neuroblastoma cell lines, and cells of the myeloid lineage. Investigation of the binding of this antibody to four different neuroblastoma cell lines showed CHP 100 bound approx four times more antibody than CHP 126. Only 30% of the cells in the line CHP 100 bound MI/N1 as determined by indirect immunofluorescence. Thus, both quantitative and qualitative differences in the expression of antigen recognized by MI/N1 are detected on human neuroblastoma cell lines. Inasmuch as only five of eight marrow aspirates heavily infiltrated with neuroblasts bound the monoclonal, this also suggests a heterogeneity in antigenic expression on fresh tumor cells. Absorption studies indicate that the antigen recognized by MI/N1 is present on human fetal brain and adult human cerebellum. At a dilution of 1/750, equal vol of fetal brain and adult cerebellum absorbed out 30 and 60% of the reactivity to the human neuroblastoma cell line CHP 100. No reactivity was found towards murine neuroblastoma cells or rat brain. Expression of antigen on cells in the myeloid lineage appears dependent upon their stage of maturation, increasing as cells mature to neutrophils and eosinophils. It is suggested that the quantitative and qualitative differences seen in the expression of antigen on neuroblastoma cells may relate to their being blocked at different stages of differentiation. (Author abstract) (28 Refs)

3. DISTRIBUTION AND MOLECULAR CHARACTERIZATION OF A CELL-SURFACE AND A CYTOPLASMIC ANTIGEN DETECTABLE IN HUMAN MELANOMA CELLS WITH MONOCLONAL ANTIBODIES.

Wilson BS, Imai K, Natali PG, Ferrone S
Dept. Molecular Immunology, Scripps Clinic Res. Foundation, 10666 North Torrey Pines Road, La Jolla, CA, 92037
Int J Cancer; 28(3):293-300 1981

The monoclonal antibodies 225.28S and 465.12 to human melanoma-associated antigens have been tested with a large variety of surgically removed skin lesions and malignant tumors as well as with a panel of cultured cell lines in serological and immunochemical assays. The antibody 225.28S reacts with a plasma membrane antigen while the antibody 465.12 detects a cytoplasmic antigen. Both antibodies fail to react with melanocytes from normal skin as well as benign skin lesions but react with nevi, melanoma cells and some skin carcinomas. Analysis with surgically removed tumors and cultured human cell lines indicated that the plasma membrane antigen is restricted to skin lesions whereas the cytoplasmic antigen is synthesized by tumor cells of various histological origins. The plasma membrane antigen is composed of two glyco-polypeptides of 280,000 and greater than 440,000 daltons, while the cytoplasmic antigen consists of four glycopolypeptides of 94,000, 75,000, 70,000 and 25,000 daltons. None of these components are bridged by disulfide bonds. The cytoplasmic antigen was readily detected in the spent culture medium of melanoma cell lines in the form of a major 94,000 dalton and a minor 72,000 dalton structure, while the plasma membrane antigen was detectable only after vastly increasing the sensitivity of the assay system. (Author abstract) (23 Refs)

4. ANTIGEN OF STRATIFIED SQUAMOUS EPITHELIUM CROSS REACTING WITH STREPTOCOCCUS A IN EPIDERMAL TUMORS.

Silagadze DG, Beletskaya LV, Bernbein BA, Kolesnikova VYu, Kogan MG, Yezhov NYa, Lampert IM
N. F. Gamaleya Inst. Experimental Medicine, USSR Acad. Medical Sciences, Moscow, USSR
Vopr Onkol; 27(6):27-32 1981

A tissue-specific basal-cell antigen of stratified squamous epithelium which enters into cross reaction with group A streptococcus polysaccharide was detected in the cytoplasm of human basal- and squamous-cell tumor cells which are associated histogenetically with skin epithelium. However, it was not found in the cells of entodermal tumors (stomach and intestinal adenocarcinoma). Considering earlier reports on the detection of cross reacting antigen in experimental ectodermal tumors, these results suggest the development of an additional histogenetical method of differential diagnosis of human tumors which arise in ectodermal tegmental epithelium. (Author abstract) (13 Refs) (In RUS)

5. EXPRESSION OF COMMON ACUTE LYMPHOBLASTIC LEUKEMIA ANTIGEN (CALLA) BY LYMPHOMAS OF B-CELL AND T-CELL LINEAGE.

Ritz J, Nadler LM, Bhan AK, Notis-McConarty J, Pesando JM, Schlossman SF
Div. Tumor Immunology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115
Blood; 58(3):648-652 1981

Previous studies have demonstrated that the common acute lymphoblastic leukemia antigen (CALLA) is expressed by leukemic cells from approx 80% of patients with non-T-cell ALL and 30%-50% of patients with chronic myelocytic leukemia in blast crisis. A small number of normal bone marrow and fetal liver cells also express CALLA, but the functional role of this molecule is unknown. In the present study, we have used a monoclonal antibody (J5) specific for CALLA to study the expression of this antigen in non-Hodgkin's lymphomas. Within the B-cell lymphomas, it was found that CALLA was expressed by almost all Burkitt's and nodular poorly differentiated lymphocytic lymphomas. Within the T-cell lymphomas, CALLA was expressed in 40% of patients with lymphoblastic lymphoma. Three of three Burkitt's lymphoma cell lines and three of eight T-lymphoblast cell lines were also found to express CALLA. Normal spleen, lymph node, and thymus cells were not reactive with J5 antibody. These findings indicate that expression of CALLA is not limited to relatively undifferentiated leukemic lymphoblasts but also occurs in more differentiated lymphoid malignancies. However, normal differentiated lymphoid cells in lymph node, spleen, and thymus, which have a phenotype similar to that of lymphoma cells, do not appear to express CALLA. (Author abstract) (26 Refs)

6. CHARACTERIZATION, BY IMMUNOPRECIPITATION, OF MYELOID- AND MONOCYTE-SPECIFIC ANTIGENS PRESENT ON THE HUMAN PROMYELOCYTIC CELL LINE (HL-60) IN THREE STAGES OF DIFFERENTIATION.

Mulder A, Alexander S, Engelfriet CP, Von dem Borne AE, Strominger JL
Dept. Immunohaematology, Central Lab. Netherlands Red Cross Blood Transfusion Service, Univ. Amsterdam, Amsterdam, The Netherlands
Proc Natl Acad Sci USA; 78(8):5091-5095 1981

The human promyelocytic leukemia cell line HL-60 is reactive with an antiserum raised against normal human granulocytes (AGS). Immunoprecipitation with AGS on [35S]methionine-labeled HL-60 cell lysates with subsequent analysis by NaDodSO4/polyacrylamide slab gel electrophoresis shows a major antigenic doublet with mol wt of 88,000 and 86,000, together with some minor antigens of lower mol wt. Upon stimulation with dimethyl sulfoxide or 12-O-tetradecanoylphorbol 13-acetate, which induces HL-60 to differentiate to mature granulocytes or monocytes/macrophages, respectively, this antigenic doublet disappears. 12-O-Tetradecanoylphorbol 13-acetate induces the synthesis of an antigen, mol wt 83,000, reactive with an antimonocyte serum. Neutrophil-specific alloantigens were not detected on HL-60 or its differentiated derivatives. (Author abstract) (29 Refs)

7. HUMAN TROPHOBLAST CELL-SURFACE ANTIGENS DEFINED BY MONOCLONAL ANTIBODIES.

Lipinski M, Parks DR, Rouse RV, Herzenberg LA
Laboratoire d'Immunologie Clinique, Institut Gustave-Roussy, 94800 Villejuif, France
Proc Natl Acad Sci USA; 78(8):5147-5150 1981

A series of monoclonal antibodies has been raised against the human choriocarcinoma cell-line, BeWo. Four antigens, Trop-1,-2,-3, and-4, are defined on normal and malignant trophoblast cells. Trop-1 and Trop-2 appear to be specifically expressed on syncytio- and cytotrophoblasts, whereas Trop-3 and Trop-4 are also detected on various tumor cell lines, normal lymphocytes, and monocytes. Anti-Trop-1 and and anti-Trop-2 antibodies might prove useful for detection and isolation of fetal trophoblast cells circulating in pregnant women's blood and for diagnosis and therapy in patients having choriocarcinomas and other germ-cell neoplasms. (Author abstract) (16 Refs)

8. BLOOD GROUP A-LIKE GLYCOLIPID AND A NOVEL FORSSMAN ANTIGEN IN THE HEPATOCARCINOMA OF A BLOOD GROUP O INDIVIDUAL.

Yokota M, Warner GA, Hakomori S
Dept. Microbiology, Hokkaido Univ. Education, Asahikawa, Hokkaido, Japan
Cancer Res; 41(10):4185-4190 1981

Two glycolipid fractions that inhibit blood group A hemagglutination were isolated from hepatocarcinoma tissue of a blood group O individual. One fraction corresponding to a ceramide penta- to hexasaccharide weakly inhibited hemagglutination caused by blood group anti-A sera and gave a precipitin reaction with Rana catesbiana lectin. The fraction had no Forssman activity, showed a single spot on thin-layer chromatography, and was degraded by hog liver alpha-N-acetylgalactosaminidase to glycolipid with a higher thin-layer chromatography mobility than that of the original glycolipid. The enzyme-treated product had no A-like activity. The direct probe mass spectrometry of the fraction after permethylation indicated the presence of the immunodominant sugar sequence GalNAc Hex HexN, but the absence of a tetrasaccharide A determinant, HexN [Fuc]Hex HexN, and a fucosyl residue. The other fraction corresponding to a ceramide di- to trisaccharide showed only a very low A-like inhibition but showed a strong Forssman activity (inhibition of sheep RBC hemolysis by anti-Forssman antibodies and complement). The activity was completely abolished by hog liver alpha-N-acetylgalactosaminidase with a simultaneous elimination of thin-layer chromatography spots, one corresponding to ceramide trisaccharide and the other with slightly higher mobility. The presence of the Forssman determinant, HexN HexN, in this fraction was clearly indicated by direct-probe mass spectrometry with a selected ion recording during continuous-temperature-gradient evaporation. Although the supply of the tumor tissue in this case was extremely limited the above information clearly indicates the presence of an aberrant A determinant and an unusual short-chain Forssman determinant in the hepatocarcinoma of the blood group O individual. The tissue did not contain normal Forssman glycolipid with a ceramide pentasaccharide structure. (Author abstract) (25 Refs)

9. THE DETECTION OF TRANSITIONAL CELL BLADDER CANCER ANTIGEN ON ESTABLISHED CELL LINES.

Boxer RJ, Sofen H, Saxon A
(c/o Saxon) Dept. Medicine, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA, 90024
Invest Urol; 19(2):70-74 1981

An antigen with mol wt of 72,000 daltons has been detected on established cell culture lines of transitional cell carcinoma. Using heterologous (rabbit) antisera and absorptions with malignant and nonmalignant cells, fetal tissues, and tissue culture proteins, we have shown that the antigen has specificity for in vitro transitional cell carcinoma. (Author abstract) (36 Refs)

10. USE OF MONOCLONAL ANTIBODIES FOR QUANTITATIVE ANALYSIS OF ANTIGENS IN NORMAL AND NEOPLASTIC TISSUES.

Brown JP, Hellstrom KE, Hellstrom I
Div. Tumor Immunology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
Clin Chem; 27(9):1592-1596 1981

We describe two methods of analyzing tissues for cell-surface antigens identified by monoclonal antibodies. The first method is a binding assay, in which a membrane fraction prepared by differential centrifugation of a tissue homogenate is incubated with 125I-labeled antibody. The specificity of the observed binding is established by competition with unlabeled antibody. The second method, double-determinant immunoassay, involves two monoclonal antibodies that recognize two distinct epitopes of the antigen molecule. An immunoadsorbent prepared from one of the antibodies is incubated with a detergent lysate of the tissue. The immunoadsorbent is then washed and incubated with the 125I-labeled second antibody. In both assays the amount of radiolabeled antibody bound is proportional to the amount of antigen in the test sample, and the limit of detection is approx 10 pg of antibody, corresponding to less than 1 fmol of antigen. (Author abstract) (17 Refs)

11. IMMUNOHISTOLOGICAL ANALYSIS OF HUMAN LYMPHOID TISSUE BY DOUBLE IMMUNOENZYMATIC LABELLING.

Mason DY, Stein H, Naiem M, Abdulaziz Z
Haematology Dept., Level 4, John Radcliffe Hosp., Oxford OX3 9DU, England
J Cancer Res Clin Oncol; 101(1):13-22 1981

A double immunoenzymatic labeling technique for the visualization of pairs of antigens on human lymphoid tissue is described along with its application to paraffin-embedded and cryostat sections of normal or neoplastic tissues. The technique is based on the reaction of rabbit anti-alkaline phosphatase (AP) with an AP substrate and the reaction of goat, sheep, or, preferably, rabbit and mouse monoclonal antibodies with a peroxidase substrate. Cells containing both immunoglobulin (Ig) kappa and lambda chains, cells containing Ig and albumin, and cells containing IgM and IgG were detected in double-labeled paraffin sections. The cells that stained for both Ig light chain classes included Reed-Sternberg and Hodgkin's cells and the giant cells in non-Hodgkin's lymphomas. The double IgM/IgG cells were rare in nonneoplastic tissue and were not found in any of the greater than 100 non-Hodgkin's lymphomas studied. The double staining of cryostat sections with monoclonal antibodies enabled the simultaneous visualization of a variety of antigen pairs (eg, T-cell antigens and IgD). The greater preservation of antigenic reaction in the cryostat sections (compared with the paraffin sections) coupled with the wide range of antigens potentially detectable with monoclonal antibodies suggested that future studies in this area will add greatly to the knowledge of the human lymphoid system. (19 Refs)

IMMUNOLOGICAL STUDIES

12. A VARIANT OF THE DEXTRAN-BINDING MOUSE PLASMACYTOMA J558 WITH ALTERED GLYCOSYLATION OF ITS HEAVY CHAIN AND DECREASED REACTIVITY WITH POLYMERIC DEXTRAN.

Matsuuchi L, Wims LA, Morrison SL
Dept. Microbiology, Columbia Univ., Coll. Physicians and Surgeons, New York, NY, 10032
Biochemistry; 20(17):4827-4835 1981

Variants have been isolated from the J558 BALB/c mouse myeloma (IgA, lambda; anti-alpha1 3dextran) that are producing immunoglobulin Ig altered in reactivity with polymeric dextran. In this report, one spontaneously raising mutant, L187, is characterized in detail. The Ig produced by L187 was indistinguishable in mol wt from that of J558; however, a difference in charge between the two proteins was observed and could be localized to the Fab portion of the molecule. Peptide map analysis failed to shown any differences between the amino acid content of the proteins; instead, the carbohydrate content of the chains differs. Examination of the glycopeptides derived from J558 and L187 Igs showed that L187 glycopeptides contain more sialic acid. Altered glycosylation apparently was the consequence of altered glycosyl-transferases within the two cell lines. Comparison of the glycopeptides from the glycoprotein G of vesicular stomatitis virus (VSV) grown in mutant and wild-type cells shows that the mutant and wild-type cells differ in their cellular glycosyltransferases. Somatic cell hybrids between either L187 or J558 and MPC-11 (4T001) also demonstrate that in the proper cellular environment the J558 protein could contain large amounts of sialic acid. J558 protein, synthesized in the hybrids and containing sialic acid, bound antigen less well than did wild-type J558 protein and identically with L87 protein synthesized in the somatic hybrids. L187 Ig does not react with polymeric dextran as well as does J558 Ig. However, the mutant Ig appears to have the same reactivity pattern with oligosaccharides as does J558, and thus the size of its antibody combining site does not appear to differ from that of J558. L187 shows that different myeloma cell lines and mutants may have different glycosyltransferases available and provides the first demonstration that the carbohydrate content of an Ig molecule can influence its reactivity with antigen. (Author abstract) (52 Refs)

13. MACROPHAGE AND T LYMPHOCYTE CONTENT OF TUMORS IN MICE TREATED WITH PROPIONI BACTERIUM.

Roszkowski K, Roszkowski W, Ko HL, Pulverer G, Jeljaszewicz J
Dept. Radiotherapy, Postgraduate Center, Sch. Medicine, Warsaw, Poland
Oncology; 38(6):334-339 1981

Macrophage and T lymphocyte content of sarcoma tumors in mice treated with Propionibacterium granulosum (PG) by different routes was investigated and compared with the effectiveness of the therapy. Two different methods for tumor macrophage detection, the Fc receptor analysis and phagocytic properties, were employed. Indirect fluorescent staining of theta-antigen on lymphocytes was used to evaluate the proportion of tumor T cells. Systemic treatment with PG appeared to be effective if given soon after tumor implantation; however, this route of administration failed to affect the tumor growth if given when the tumor was already advanced. The therapeutic efficiency of intralesional PG injection was almost as effective as early systemic treatment. We obtained evidence indicating that effectiveness of PG therapy was associated with an increase of the macrophage and T cell content of tumors. (Author abstract) (31 Refs)

14. QUANTITATIVE IMMUNOFLUORESCENT ANALYSIS OF SURFACE PHENOTYPES OF MURINE B CELL LYMPHOMAS AND PLASMACYTOMAS WITH MONOCLONAL ANTIBODIES.

Lanier LL, Warner NL, Ledbetter JA, Herzenberg LA
Immunology Lab., Dept. Pathology and Medicine, Univ. New Mexico Sch. Medicine, Albuquerque, NM, 87131
J Immunol; 127(4):1691-1697 1981

In this study, a large series of murine B lymphomas and plasmacytomas were examined by quantitative flow cytometry analysis using a panel of monoclonal antibodies against murine differentiation antigens. These cell lines appear to represent subpopulations of lymphoid cells arrested at distinct stages of differentiation. In general, the pattern of reactions of these monoclonal antibodies with the B cell neoplasms was comparable to the reactions seen with normal cells in the same lineage. The Thy-1.2, Lyt-2, and T-30 differentiation antigens were not detected on any B lymphoma or plasmacytoma. However, certain surface Ig-positive B lymphomas do express the Lyt-1 antigen. With respect to other differentiation markers examined, including E2, F1, ThB, Lgp-100 (Ly 9.1), G2, and T-200 (Ly 5), the reaction of the B cell tumors reflected the expression of these markers on comparable normal cells. This investigation also emphasized the marked intratumor and intertumor heterogeneity that is observed when cloned cell lines are analyzed quantitatively for a large number of surface markers. Thus, this approach may be particularly useful in defining heterogeneity in maturation states within cloned tumor cell lines. (Author abstract) (33 Refs)

15. SURFACE MEMBRANE ANTIGENS OF HEMOPOIETIC TUMOR CELL LINES AND NORMAL MARROW PROGENITOR CELLS.

Hasthorpe S, Rogerson J, McKenzie IF
Cancer Inst., 481 Little Lonsdale St., Melbourne, 3000, Australia
Cancer Res; 41(10):3985-3991 1981

A xenoantiserum raised against a mast cell tumor line (FMP1.1) was found to have cross-reactivity with surface antigens on primitive hemopoietic precursor cells in normal mouse bone marrow: erythroid burst-forming units; granulocyte-macrophage colony-forming cells; and high-proliferative-potential granulocyte-macrophage colony-forming cells. In the presence of anti-FMP1.1 serum and complement, only 15 +-2% (S.E.) (n = 5) of normal nucleated marrow cells were lysed, demonstrating that the majority of mature hemopoietic cells did not express the antigens detected on their primitive counterparts. A variety of hemopoietic and other tumor cell lines were examined with anti-FMP1.1 serum, and all B- and pre-B-lymphomas, one plasmacytoma, one mastocytoma, and a monocyte-macrophage line exhibited significant lysis. Direct typing of the FMP1.1 tumor demonstrated that it did not express the B-cell surface antigens such as Ia, surface Ig, Fc, and complement (C3) receptors. Although the Ly.6 alloantigen was present on FMP1.1 cells, this antigen was not found on marrow erythroid burst-forming units and granulocyte-macrophage colony-forming units. Absorption of anti-FMP1.1 serum with cross-reacting (WEHI-3 and W-279.1) and a nonreacting (P-815) cell line confirmed the specificity of the antiserum reaction with these cells and marrow progenitors. These experiments indicated that more than one antibody is contained in anti-FMP1.1 serum. Thus, the mast cell tumor (FMP1.1) carries an unusual array of antigens, which are found on bone marrow progenitors and are not expressed on the majority of differentiated cells. It has been demonstrated that tumor cell lines provide an important basis for the analysis of surface membrane antigens expressed on normal hemopoietic progenitors. (Author abstract) (29 Refs)

16. EXPRESSION OF HETEROPHILE PAUL-BUNNELL ANTIGEN ON HUMAN LYMPHOID CELL LINES.

Sugisaki T, Kano K, Minowada J, Milgrom F
Dept. Microbiology, State Univ. New York at Buffalo, Sch. Medicine, Buffalo, NY, 14214
Clin Immunol Immunopathol; 21(1):77-82 1981

Thirty-eight human hematopoietic cell lines were studied for the expression of heterophile Paul-Bunnell (P-B) antigen by means of indirect immunofluorescence tests. Of five normal B-cell lines of Oriental origin, three showed very high and two moderate increase in number of cells stained for IgM after preincubation with infectious mononucleosis (IM) sera. In contrast, of nine normal B-cell lines of Caucasian origin, none showed high and only two showed moderate increase of cells stained for IgM. The remaining seven cell lines did not show any such increase. Of 24 cell lines from patients with proliferative diseases of hematopoietic cells, 17 Caucasian, 6 Negro and 1 Oriental, only 3 myeloma cell lines, all of Caucasian origin, showed significant increase of stained cells. Absorption experiments as well as mixed agglutination studies showed that antibodies in the IM sera combining with cell lines are of P-B specificity and not of any other heterophile specificity. (Author abstract) (11 Refs)

17. THE ANALYSIS OF LYMPHOID SUBPOPULATIONS IN NORMAL AND MALIGNANT TISSUES BY IMMUNOFLUORESCENE TECHNIQUE.

Janossy G, Thomas JA, Pizzolo G
Dept. Immunology, Royal Free Hosp., Sch. Medicine, Hampstead, London NW3, London
J Cancer Res Clin Oncol; 101(1):1-11 1981

Antibodies labeled with fluorescein isothiocyanate and tetraethylrhodamine isothiocyanate were used to analyze the cellular composition of normal lymphoid tissues and 40 non-Hodgkin's lymphomas by immunofluorescence (IF) in frozen tissue sections. The antisera tested included conventional reagents to immunoglobulin classes, human thymocyte (T cell) and Ia-like antigens, and monoclonal antibodies including the OKT antibodies that react with T-cell subpopulations. The IF technique was found to give an accurate analysis of the normal and malignant cells and to yield information complementary to conventional histology. In normal tissues, the combination of antisera to Ia-like antigens and T lymphocytes made it possible to identify reticular cells corresponding to interdigating (ID) cells in peripheral lymphoid tissue. Membrane antigens on ID cells, lamina propria macrophages, and lymphocytes were labeled with a monoclonal antibody to human WBC antigen. Reagent combinations that simultaneously recognized T and B lymphoid cells revealed intriguing variations in the proportion and location of the T cells in B-lymphomas. In some patients, large proportions of T lymphocytes and blasts were clearly seen in close contact with B cells of variable size. Further studies with antibodies to T-cell subsets of inducer and suppressor functions should reveal the clinical significance of these findings. (39 Refs)

18. ANALYSIS OF THE NONVIRAL ANTIGENS IMMUNOPRECIPITABLE BY SV40 T ANTIBODY FROM SV40-TRANSFORMED HUMAN/MOUSE HYBRID CELL LINES.

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Virology; 114(1):149-160 1981

The expression of nonviral antigens, ie, host-coded proteins with mol wt from 48,000-56,000 (48K-56K) immunoprecipitable from extracts of simian virus 40 (SV40)-infected or -transformed cells by anti-SV40 tumor antibody, was examined in four SV40-transformed human cell lines, one SV40-transformed mouse cell line, and eight SV40-transformed human/mouse somatic cell hybrid cell lines produced by fusion of SV40-transformed human cells with untransformed mouse cells. Differences were found in the patterns of expression of these viral induced proteins among the human cell lines, between the human and the mouse cell lines, and between the human/mouse somatic cell hybrid cell lines and the human lines from which they were derived. Two of the human cell lines expressed only a 55K nonviral antigen; two expressed both a 55K and a 52K nonviral antigen. The mouse cell line expressed both a 55K and a 48K nonviral antigen. Each hybrid cell line expressed a 55K and also a 48K nonviral antigen, except one. The BALB IV-8 hybrid cell line expressed 55K and 52K nonviral antigens. By comparing the tryptic peptides fractionated on cation exchange columns of the nonviral antigens we determined: (1) the 48K nonviral antigen in human/mouse hybrids is encoded by a mouse chromosome. (2) The 52K nonviral antigen in the BALB IV-8 human/mouse hybrid is encoded by a mouse chromosome. It is possibly a precursor to the mouse 48K protein because it contains one extra tryptic peptide in addition to those of the mouse 48K protein, because one peptide has an altered mobility and because the 52K protein is found, so far, only in a human/mouse hybrid that does not exhibit a 48K nonviral antigen. (3) The 55K nonviral antigen in the C57-VII-6 human/mouse hybrid is encoded by a human chromosome. In the BALB IV-8 human/mouse hybrid, there is a 55K protein encoded by a human chromosome and probably a 55K protein encoded by a mouse chromosome. (4) If the gene encoding the human 55K nonviral antigen is located on a single chromosome, it is located on human chromosome 7. (Author abstract) (25 Refs)

VIRUS ASSOCIATED ANTIGENS

19. NONDETECTION OF INFECTIOUS HEPATITIS B VIRUS IN A HUMAN HEPATOMA CELL LINE PRODUCING HEPATITIS B SURFACE ANTIGEN.

Tabor E, Copeland JA, Mann GF, Howard CR, Skelly J, Snoy P, Zuckerman AJ, Gerety RJ
Bureau Biologics, 8800 Rockville Pike, Bethesda, MD, 20205
Intervirology; 15(2):82-86 1981

The PLC/PRF/5 human hepatoma cell line producing hepatitis B surface antigen (HBsAg) was studied to determine whether infectious hepatitis B virus (HBV) was also being produced. Two chimpanzees with no previous exposure to HBV and no serologic markers of past or active HBV infection were inoculated iv with 50 ml of either tissue culture supernatant fluid (357 ng/ml HBsAg) or a suspension of cells disrupted by repeated freeze-thaw cycles (57 ng/ml HBsAg). No evidence of HBV infection was detected in either chimpanzee during 6 mo of evaluation. This study suggests that the expression of a portion of the HBV genome, when a portion or all of that genome has been incorporated in a host cell, can result in the production of HBsAg without infectious HBV. If it becomes possible to produce a similar expression of this portion of the genome by itself in nonmalignant cells, HBsAg without HBV may be produced in vitro for use in hepatitis B vaccines. (Author abstract) (21 Refs)

20. INHIBITION OF ADENOVIRUS-TRANSFORMED CELL ONCOGENICITY BY ADENO-ASSOCIATED VIRUS.

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Dept. Microbiology, Johns Hopkins Univ., Sch. Medicine, Baltimore, MD, 21205
Virology; 113(2):521-533 1981

Adeno-associated virus (AAV) has been shown to inhibit the oncogenicity and transforming ability of adenovirus (Ad). Using the H14b Ad-transformed hamster cell line, we have developed a model system in which to characterize the molecular events responsible for these inhibitory effects. AAV infection of H14b cells decreases their oncogenicity by approx threefold. The tumors that do arise are significantly smaller and have a longer latent period. AAV infection also alters the in vitro properties of the H14b cells, reducing cloning efficiency in methyl cellulose by 38-92% and saturation density by two- to four-fold. The molecular basis of this inhibition appears to be an inhibition of production of the 58K tumor antigen as determined by fluorescent antibody and immunoprecipitation studies. The reduction in the levels of tumor antigens are not due to alterations or loss of the Ad genome within H14b cells but may reflect an alteration in transcription or processing of Ad-specific mRNA. AAV infection of H14b cells does not lead to detectable levels of AAV DNA synthesis, but some AAV transcripts are made. This is the first instance in which AAV transcription has been detected in an Ad-transformed cell line. (Author abstract) (42 Refs)

21. ASSOCIATION OF EPSTEIN-BARR VIRUS WITH NASOPHARYNGEAL CARCINOMA IN ALASKAN NATIVE PATIENTS: SERUM ANTIBODIES AND TISSUE EBNA AND DNA.

Lanier AP, Bornkamm GW, Henle W, Henle G, Bender TR, Talbot ML, Dohan PH
Alaska Investigation Div., Centers for Disease Control, 225 Eagle St., Anchorage, AK, 99501
Int J Cancer; 28(3):301-305 1981

Biopsy specimens from Alaskan Native patients with nasopharyngeal carcinoma (NPC) and from other patients seen on the otolaryngology service were tested for Epstein-Barr virus-specific DNA and nuclear antigen (EBNA). Serum samples from both groups were tested for various EBV-related antibodies. EBV DNA and EBNA results were in agreement in 29 of 31 tissue specimens tested by the two methods. Ten of 11 biopsies containing NPC cells were positive for EBV DNA. Two NPC patients had biopsies that showed only atypical epithelium but were also positive for EBV DNA or EBNA. The other tissue specimens were negative except for biopsies from two patients: one with a parotid gland lymphoepithelial lesion; another with undifferentiated carcinoma of salivary gland origin. (Author abstract) (28 Refs)

22. DEMONSTRATION OF ANTIGENIC CROSS-REACTIVITY BETWEEN SIMIAN SARCOMA VIRUS (SSV) AND MASON-PFIZER MONKEY VIRUS (MPMV). BRIEF REPORT.

Micheel B
Central Inst. Cancer Res., Lindenberger Weg 80, DDR-1115 Berlin-Buch, E. Germany
Arch Virol; 69(2):149-153 1981

The reaction of FITC-labeled simian sarcoma virus (SSV) with anti-SSV p30 antibodies conjugated to Sepharose beads is specifically blocked by incubation with antisera to different Type-C virus p30s and also by anti-MPMV p27 serum. (Author abstract) (14 Refs)

23. DEMONSTRATION OF SV40-RELATED TUMOUR ANTIGEN IN HUMAN MENINGIOMAS BY DIFFERENT HAMSTER SV40-T-ANTISERA.

Zimmermann W, Scherneck S, Geissler E, Nisch G
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Acta Virol (Praha); 25(4):199-204 1981

Three of five human meningiomas tested in cell culture expressed SV40-related tumor (T) antigen as measured by indirect immunofluorescence with four different hamster anti-SV40 tumor sera. The percent of T-antigen-positive nuclei varied depending on the antisera used. In one case (meningioma G S), only 25% of the T-antigen-positive nuclei detected with one antiserum could be demonstrated with another serum. The possible explanations are discussed. None of the meningioma cell cultures tested expressed SV40-related viral capsid (V) antigen. (Author abstract) (20 Refs)

24. SV40 ANTITUMOR SERA THAT DIRECTLY IMMUNOPRECIPITATE SMALL-T-ASSOCIATED CELLULAR PROTEINS.

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Virology; 114(1):297-301 1981

Two cellular proteins, 56K and 32K, are immunoprecipitated in association with SV40 small-t antigen using antisera from animals bearing SV40-induced tumors. Antitumor sera have now been identified that immunoprecipitate these proteins directly from uninfected, as well as infected, cells. (Author abstract) (10 Refs)

25. MONOCLONAL ANTIBODIES SPECIFIC FOR SIMIAN VIRUS 40 TUMOR ANTIGENS.

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Dept. Molecular Virology, Imperial Cancer Res. Fund Lab., London WC2A 3PX, England

J Virol; 39(3):861-869 1981

Thirty hybridomas that secrete Ig against the simian virus 40 tumor antigens were isolated and cloned. Of these, 28 produced antibodies which bound to simian virus 40 large-T, and 2 produced antibodies which bound to the host 53,000-dalton protein. As in previous work, large-T antigen was found to have at least one determinant that it shared with small-t antigen and to have a minimum of six unique determinants. Several of the monoclonal antibodies from the L series hybridomas recognized determinants that were present on a subset of the large-T antigen from simian virus 40-transformed mouse cells. These monoclonal antibodies should be useful in studies of the structure and function of the simian virus 40 tumor antigens. (Author abstract) (30 Refs)

26. IMMUNOSELECTION OF SIMIAN VIRUS 40 LARGE T ANTIGEN MESSENGER RNAS FROM TRANSFORMED CELLS.

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Virology; 113(2):790-793 1981

The messenger RNAs (m-RNAs) coding for the simian virus 40 (SV40) large tumor antigen were substantially purified by immunoprecipitation of polysome fractions from SV40-transformed cells. The level of SV40 T antigen m-RNA in the transformed cell used in this study was estimated at 0.05% of the total population of polyadenylated m-RNAs and a several-hundred-fold purification of this m-RNA was achieved by employing antibodies to SV40 large T antigen purified by either of two methods. The procedures described in this communication should be particularly useful for the immunoselection and purification of low-abundance m-RNAs or when the antigen is not available in large quantities. (Author abstract) (12 Refs)

27. FUNCTIONS OF T ANTIGENS OF SV40 AND POLYOMAVIRUS.

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Biochim Biophys Acta; 651(1):1-24 1981

Functions of the tumor or T antigens of SV40 and polyomavirus are reviewed. Topics discussed include genome organization (SV40 genome, polyomavirus genome, and comparison of maps), proteins of the early regions (SV40 antigens, polyomavirus T antigens, and super T antigens), functions of T antigens (small t antigen, middle T antigen, and large T antigen), other immunoreactive T antigens (tumor-specific transplantation antigens, U antigen, and cellular proteins bound by antibodies against SV40 T antigens), large T antigen binding to DNA, viral DNA synthesis, cellular DNA synthesis (SV40 and polyomavirus), adenovirus helper function, regulation of viral transcription, integration of viral DNA, enzyme reactivities associated with T antigens (SV40 and polyomavirus), T antigens and transformation (SV40, polyomavirus, and A and N transformants), and conclusions. (196 Refs)

TUMOR ASSOCIATED TRANSPLANTATION ANTIGENS

28. ERADICATION OF DISSEMINATED MURINE LEUKEMIA BY CHEMOIMMUNOTHERAPY WITH CYCLOPHOS PHAMIDE AND ADOPTIVELY TRANSFERRED IMMUNE SYNGENEIC LYT-1 + 2- LYMPHOCYTES.

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J Exp Med; 154(3):952-963 1981

The efficacy of T cell subpopulations, as distinguished by expression of Lyt antigens, was analyzed in adoptive chemoimmunotherapy (ACIT) of established murine leukemia and in in vitro assays for the generation and expression of cytotoxicity. The results demonstrated that the predominant donor effector cell required for eradication of advanced disseminated leukemia by ACIT is an immune Lyt-1+2-T cell that is not cytolytic in vitro. Immune cells depleted of Lyt-2+ cells, such that the only donor T cells remaining were of the Lyt-1+2-phenotype, were nearly as effective in ACIT as unselected cells suggesting that other donor T cell subsets do not provide an essential contribution. The potential therapeutic efficacy of immune cells was ablated nearly as completely by depletion of Lyt-1+ cells as by depletion of all T cells. The small residual anti-tumor effect still evident after treatment of immune cells with alpha-Thy-1.2 and complement probably reflected incomplete T cell removal. The T cell subset analyzed in ACIT were defined operationally by susceptibility to lysis by monoclonal antibody to Lyt antigens and complement. The results demonstrated that the phenotype of the predominant T cell subset required for efficacy in ACIT is Lyt-1+2-, which is distinct from the T cell phenotypes mediating in vitro tumor lysis. The mechanisms by which Lyt-1+2-cells can promote tumor rejection are discussed. (31 Refs)

29. A SURVEY OF ETHYLNITROSOUREA-INDUCED RAT GLIOMAS FOR THE PRESENCE OF TUMOUR REJECTION ANTIGENS EXPRESSED IN VIVO.

Spence AM, Priestley G
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Neuropathol Appl Neurobiol; 7(1):63-75 1981

Seven malignant gliomas induced in F-344 rats with transplacentally-induced ethylnitrosourea (ENU) using conventional transplantation assays were tested for tumor rejection antigens. Assay for tumor rejection antigens of syngeneic rats was attempted by ligation or excision of tumor grafts, or by inoculation of radiation-killed tumor cells or live tumor cells at sublethal doses. Groups were then challenged with viable tumor cells and tumor outgrowth compared to that in control groups. In 4/5 cell lines the tumor ligation method was unusable because of high incidence of local tumor recurrences or metastases. Heavily irradiated cell suspensions exposed to 60Co (15,000 rad) were used for immunization of six of the glioma lines. Despite the irradiation, inocula produced palpable nodules before regression. After a series of immunizing injections, challenge was performed 7-18 days after the last immunization. The o utgrowths in two cases (a cerebral glioblastoma and cerebral mixed astrocytoma-ependymoma) indicated tumor rejection responses. Immunization with a mixed oligodendroglioma-astrocytoma and two glioblastoma multiforme led to enhanced outgrowth of challenge cell inocula. The remaining two tumors, a glioblastoma multiforme and a mixed astrocytoma-oligodendroglioma, showed neither rejection nor enhancement response. Immunization with a 3-methylcholanthrene-induced urinary bladder carcinoma line had no effect on the outgrowth of six of the glioma cell lines. ENU-induced malignant rat gliomas apparently do not uniformly elicit strong tumor rejection responses in vivo. (42 Refs)

30. SYNGENEIC IMMUNE RESPONSE TO RAT TRACHEAL EPITHELIAL CELLS TRANSFORMED IN VITRO BY N-METHYL-N-NITRO-N-NITROSOGUANIDINE.

Braslawsky GR, Steele V, Kennel SJ, Nettesheim P
Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830
Br J Cancer; 44(2):247-257 1981

Two cell lines (2-10-1 and 8-10-2) derived by exposure of primary tracheal explants to MNNG in vitro were not tumorigenic in syngeneic F-334 rats or athymic BALB/c (nu/nu) mice at early passage, but became tumorigenic at late passage. These cell lines are therefore suited to study the expression of neoantigens during neoplastic development. Transplantation resistance to late-passage, tumorigenic cells was induced in syngeneic rats using an immunization protocol of repeated cell inoculation and tumor ablation. Spleen cells from such animals were reactive in 20h microcytotoxicity assays against neoplastic cell lines, but unreactive to normal tracheal epithelial cells. Similarly, immune spleen cells co-cultivated in vitro for 6 days with irradiated neoplastic cell lines before assay for microcytotoxicity were strongly reactive, whereas co-cultivation with normal epithelial cells did not stimulate reactivity. Antibody to these neoplastic cell lines was demonstrated in sera of tumor-resistant rats by an indirect radiolabeled-antibody binding test and by indirect immunofluorescence. There was no significant binding to normal tracheal epithelial cell outgrowths. (Author abstract) (28 Refs)

31. PREFERENTIAL GROWTH OF MAMMARY TUMORS IN INTACT MAMMARY FATPADS.

Miller FR, Medina D, Heppner GH
Dept. Immunology, Michigan Cancer Foundation, 110 East Warren Ave., Detroit, MI, 48201
Cancer Res; 41(10):3863-3867 1981

Four transplantable mammary tumors, three (66, 410, and 168cl) isolated from a spontaneously occurring strain BALB/cfC3H mammary tumor and one (D2) arising from a BALB/c hyperplastic alveolar nodule were found to grow better in mammary fatpads than at sc sites. Furthermore, tumor growth was better (p less than 0.05) in intact mammary glands than in cleared mammary fatpads from the D2, 410, and 66 tumors (168cl was not tested). The role of immunity in these differences was investigated using the highly immunogenic 410 tumor. Tumor 410 induced equally effective immunity to subsequent challenge whether it was implanted sc or in intact fatpads. Furthermore, in immunized animals, Tumor 410 was rejected equally well when the challenge site was intact fatpad as when sc. Similarly, Tumor 410 induced immunity after implantation into cleared fatpads and, in immunized animals, were rejected when the challenge site was the cleared fatpad. We thus found no evidence that the mammary fatpad is immunologically privileged, as compared to the sc site, with respect to tumor transplantation antigens. (Author abstract) (21 Refs)

CLINICAL DIAGNOSTIC STUDIES

32. DEMONSTRATION WITH MONOCLONAL ANTIBODIES OF AN UNUSUAL MONONUCLEAR CELL INFILTRATE AND LOSS OF NORMAL EPITHELIAL MEMBRANE ANTIGENS IN HUMAN BREAST CARCINOMAS.

Daar AS, Fabre JW
Nuffield Dept. Surgery, Univ. Oxford, John Radcliffe Hosp., Oxford OX3 9DU, England
Lancet; 2(8244):434-438 1981

Monoclonal antibodies to two differentiation antigens normally expressed on the membranes of breast epithelial cells were used in immunofluorescence studies on frozen sections of malignant breast tumors. It was demonstrated that most tumors did not express these antigens on their cell membranes, and it was possible to classify histologically indistinguishable tumors according to whether they expressed the antigens. The absence of these membrane antigens is likely to be a subtle indicator of cellular differentiation and to have metabolic and other functional implications for the tumor. The demonstration that otherwise indistinguishable tumors can be classified in this way therefore has obvious potential for clinical exploitation. In addition, it was demonstrated that the majority of the mononuclear cells in those tumors with intense mononuclear cell infiltrates expressed an antigen not normally found on mature lymphocytes and macrophages. (Author abstract) (11 Refs)

33. ANALYSIS OF SERA FROM BREAST CANCER PATIENTS BY RADIOIMMUNOASSAYS.

Davis JW, Olive M, Cailleau R, Bowen JM
Dept. Molecular Carcinogenesis and Virology, Texas Medical Center, Univ. Texas System Cancer Center, MD Anderson Hosp. and Tumor Inst., Houston, TX, 77030
Cancer Immunol Immunother; 11(3):225-231 1981

Sera from 324 breast cancer patients were tested against various cell lines, including four human breast cancer, four human non-breast cancer, and three animal cell lines. Antibody reactivity was measured indirectly by binding antibodies to I125-labeled protein and directly using I125-labeled antibodies. Sera from 30 patients showed positive results, with nine different patterns of reactivity. Of these sera, two samples reacted positively only to human breast cell lines MDA-MB231 and MDA-MB330. Fifteen of the remaining 28 samples reacted with animal as well as human cell lines. Evidently breast cancer patients are sensitized to antigens occurring on breast cancer cells more often than normal individuals. Several different types of antigens, not all of which are specific to breast cancer cells, are detected by sera from such patients. The types of sera reactive only against breast cancer cell lines may be useful for the analysis of tumor-associated antigens. (36 Refs)

34. DIAGNOSIS OF BREAST CARCINOMA WITH THOMSEN-FRIEDENREICH (T) ANTIGEN AND HUMAN ANTI-T ANTIBODY.

Springer GF, Murthy SM, Desai PR, Wurtz K, Black S, Scanlon EF
Dept. Surgery, Northwestern Univ., Evanston, IL
Breast; 7(3):24-30 1981

Delayed-type skin hypersensitivity (DTH) to T antigen was measures in 102 patients with ductal breast carcinoma, 24 patients with lobular and two patients with tubular breast carcinoma, and 148 patients with benign breast diseases. Cell-mediated T antigen immunity was measured in vitro by leukocyte migration inhibition. T-specific immunoreactive structures were found on 93% of breast carcinoma tissues, all distant metastasis tissues, all cultured breast carcinoma-derived cell lines, on adenocarcinoma tissues from other sites, and on four out of six melanomas. T-specific structures were not detected in 29 of 31 benign breast lesions or any of four mammoplasty tissues. Patients showing apparent false positives had hyperplastic conditions, which were later rediagnosed as carcinomas. Data from patients after surgery suggest that T-specific DTH may be useful in monitoring treatment of breast cancer treatment, since DTH disappears in patients not showing recurrence of tumors. Apparently T-specific structures occur in normal tissues in a covered form. In adenocarcinoma tissues these structures are in an exposed, reactive form, which may serve diagnostic purposes. The T antigen may be useful in adjuvant therapy. (31 Refs)

35. LOCALIZATION OF MAMMARY TUMORS IN VIVO WITH 131I-LABELED FAB FRAGMENTS OF ANTIBODIES AGAINST MOUSE MAMMARY EPITHELIAL (MME) ANTIGENS.

Wilbanks T, Peterson JA, Miller S, Kaufman L, Ortendahl D, Ceriani RL
(c/o Peterson) Bruce Lyon Memorial Res. Lab., Children's Hosp. Medical Center, 51st and Grove St., Oakland, CA, 94609
Cancer; 48(8):1768-1775 1981

The Fab fragments of antibodies against cell-type-specific surface antigens of mouse mammary epithelial cells (MME-antigens) were used to localize mammary tumors successfully. The radioiodine-labeled anti-MME (Fab) was injected into mice carrying simulated mammary metastases, and after 24 hr the amounts of label per gram of excised tissue was several times greater in the tumor than in liver, brain, lung, or muscle. Kidney showed considerable accumulation of label but this appeared to be nonspecific. Kinetic studies revealed a rapid elimination of labeled Fab in the urine with only 1% of the injected dose remaining in the entire blood pool after 24 hr. With a high-purity germanium camera, mammary tumors were clearly located by the 131I-labeled anti-MME (Fab), and normalization to 99mTc-pertechnetate distribution in the animal increased the specificity. The density of 131I-label was fourfold greater over the mammary tumor than over comparable areas of the mouse. No accumulation of 131I-anti-MME (Fab) was observed in nonmammary tumors nor in mammary tumors when labeled nonspecific Fab was used. An analogous system using an anti-human mammary epithelial antiserum is being developed for localization of breast metastases in humans. (Author abstract) (40 Refs)

36. SECRETORY-COMPONENT-PRODUCING LUNG CANCER WITH HYPERGAMMAGLOBULINEMIA OF SECRETORY IGA.

Gotoh T, Takishita Y, Doi H, Tsubura E
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Cancer; 48(8):1776-1782 1981

Studies were made on a case of well-differentiated adenocarcinoma of the lung in which the serum levels of secretory IgA (sIgA) were very high. Immunofluorescent studies showed that secretory component (SC) was found to be diffusely distributed in cancer cells. The SC was detected in the supernatant of homogenates of cancer tissues from the primary site and lymph node with metastases. The SC extracted from cancer tissue and purified colostral SC were antigenically identical. The authors conclude that the adenocarcinoma cells produced SC and secreted it into the bloodstream and that the binding of SC with polymeric IgA resulted in the hypergammaglobulinemia of sIgA. This appears to be the first reported case of SC-producing lung cancer. The authors' findings suggest that the high serum levels of sIgA in cancer patients may be due to the production and secretion of SC by tumor cells themselves rather than the reabsorption of intraluminal sIgA into the circulation through a damaged epithelium. (Author abstract) (28 Refs)

37. ANTI-IA-REACTIVE CELLS IN MYCOSIS FUNGOIDES: A STUDY OF SKIN BIOPSIES, SINGLE EPIDERMAL CELLS AND CIRCULATING T LYMPHOCYTES.

Tjernlund UM, Scheynius A, Kabelitz D, Klareskog L
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Acta Derm Venereol (Stockh); 61(4):291-301 1981

Skin sections, epidermal cells in suspension and circulating T lymphocytes were investigated for the presence of Ia-like antigens in a group of patients with the cutaneous T-cell lymphoma mycosis fungoides (MF) and in healthy controls. Highly purified anti-Ia antibodies were used in indirect immunofluorescence, indirect peroxidase and peroxidase-antiperoxidase techniques. Allogeneic and autologous mixed leukocyte reaction tests with epidermal cells from MF lesions as stimulator cells were also performed. The majority of the dermal lymphohistiocytes and mononuclear cells in the epidermal Pautrier microabscesses expressed Ia-like antigens. So also did a greater proportion of circulating T lymphocytes than in the controls. In some MF patients a high percentage of single epidermal cells of non-lymphoid character also reacted with the antibodies. The possible significance of the present findings for the pathogenesis of MF is discussed. (Author abstract) (30 Refs)

38. ETIOLOGICAL IMPLICATIONS ON KAPOSI'S SARCOMA.

Giraldo G, Beth E, Kyalwazi SK
Natl. Cancer Inst. 'Fondazione Pascale', Naples, Italy
Antibiot Chemother; 29:12-29 1981

Multidisciplinary study of 176 cases of Kaposi's sarcoma (KS) was conducted during 1971-1979. Biopsy specimens and sera from KS patients and corresponding controls were collected within five different African Cancer Centers in areas of high and moderate KS incidence. Samples were also collected in various hospitals in areas of France with a low incidence of KS. African KS patients had high antibody titers to cytomegalovirus (CMV), but they were not significantly different from controls in the same regions. A specific serological association of European and American KS with CMV was established. CMV-related antigens were detected in 22% of tumor biopsies and in early passages of cell cultures derived from them. CMV-DNA sequences have been detected in tumor biopsies. Strain K9V CMV has been isolated in a KS-derived tissue culture. In vitro, cells infected with K9V have some of the features of cells transformed by other oncogenic CMV strains. In vivo, K9V induced a fatal lymphoid disease in old world monkeys. Clusters of KS have been observed in the West Nile District of Uganda. A significantly higher incidence of second primary tumor, particularly of the lymphoreticular system, has been observed in KS patients. (32 Refs)

39. FUNDAMENTALS OF A SPECIFICALLY-ACTIVE IMMUNE THERAPY FOR MALIGNANT MELANOMAS.

Mutzner PA, Stuhlmiller GM, Seigler HF, Stumpf WE, Sar M
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Schweiz Med Wochenschr; 111(36):1322-1325 1981

Since Morton demonstrated in 1968 that malignant melanoma is antigenic, many immunologists have taken an interest in this disease. A basis for specific active immunotherapy has been worked out at Duke University Medical Center, Durham, NC (USA). A female chimpanzee was hyperimmunized with melanoma cells grown in tissue culture. After appropriate absorptions the xeno-antiserum was tested by indirect immunofluorescence. Apart from unspecific activities in the serum detectable against normal human fetal and adult fibroblasts as well as other non-melanotic human tumors, following further absorptions with these cells a melanoma-specific antigen could be demonstrated on the surfaces of melanoma cells. The melanoma-specific tumor-associated antigens were further evaluated by direct and indirect immunoautoradiography. These studies suggest that there are indeed cross-reacting specific tumor-associated antigens on the cell surface of melanoma cells. At DUMC melanoma patients have therefore been hyperimmunized with melanoma cells + BCG. Clinical experience is discussed. (Author abstract) (13 Refs) (In GER)

40. IMMUNOHISTOLOGICAL ANALYSIS OF HODGKIN'S AND STERNBERG-REED CELLS: DETECTION OF A NEW ANTIGEN AND EVIDENCE OF SELECTIVE IGG UPTAKE IN THE ABSENCE OF B CELL, T CELL AND HISTIOCYTIC MARKERS.

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J Cancer Res Clin Oncol; 101(1):125-134 1981

The results of studies to clarify the origin and nature of Hodgkin's (H) and Sternberg-Reed (SR) cells are presented. Cytoplasmic IgG (CIgG) was demonstrated by immunostaining in polymorphic astrocytomas, liver cell carcinomas, and other polymorphic neoplasms as well as in H and SR cells. In addition, human IgG was taken up by rat liver cells, but alpha1 antitrypsin was not. These results showed that CIgG cannot be used as a marker for histiocytes. Staining of frozen sections revealed that H and SR cells lacked surface Igs and peripheral T-cell antigen. An antiserum raised against Hodgkin's disease (HD) L 428 cells and absorbed with normal human cells reacted strongly with H and SR cells in frozen sections of HD-affected lymph nodes. In 10 cases, the antiserum stained the surface of the H and SR cells; in 2 cases, it also stained the nucleoli and some chromatin spots. The antiserum did not react with tonsil tissue cells (lymphoid cells, histiocytes, interdigating reticulum cells). It was concluded that the nature of the H and SR cells is still open and that these cells might express antigens that have not yet been detected on normal cells. (29 Refs)

41. HETEROGENEITY OF LYMPHOBLASTIC MALIGNANCIES IN CHILDREN.

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J Cancer Res Clin Oncol; 101(1):23-27 1981

Lymphocyte surface markers were studied in 6 children with null cell lymphoblastic lymphomas (LLs), 16 with T cell LLs, and 15 children with B cell LLS. The null cell tumors showed a phenotype of acute lymphoblastic leukemia (ALL) antigen+ Ia antigen+ and terminal deoxyribonucleotidyl transferase (TdT)+. The T cell tumors showed three major phenotypic subgroups: HTLA+, E rosette-, TdT+, and occasional ALL cells (prethymic phenotype); E rosette+, HTLA+, and Tdt+ (thymic cortical phenotype); and E rosette+-, HTLA+, complement 3d+, and TdT- (fetal thymic phenotype). Most B cell tumors had the phenotype of surface IgM immunoglobulins with or without cytoplasmic IgM, and which may express ALL antigen. A small group of B cell tumors expressed the surface IgM and complement 3d phenotype reminiscent of adult follicular lymphoma. The phenotypic heterogeneity found in these children indicated that further studies will be needed before an adequate histologic and phenotype classification of these malignancies can be developed. (no Refs)

42. CLASSIFICATION OF ACUTE LEUKEMIA BY SURFACE MARKERS AND CORRELATION WITH DIAGNOSTIC MORPHOLOGIES. RESULTS OF 111 CASES.

von Fliedner V, Carrel S, Morell A, Heumann D, Losa G, Hirt A, Jeannet M, Mach JP, Cruchaud A
Division d'immunologie et d'allergologie, Hopital cantonal universitaire, CH-1211 Geneve 4, Switzerland
Schweiz Med Wochenschr; 111(41):1524-1526 1981

One hundred eleven patients with acute leukemia, including 29 children, were classified according to the surface markers and cytochemistry of their blasts. The acute leukemias were separated into two major groups (lymphoid and non-lymphoid) depending on the presence or absence of specific lymphoid markers. On the basis of these criteria a correlation of 94% with the hematological diagnosis was obtained. Acute lymphoblastic leukemia (ALL) was divisible into three sub-groups: 11 cases expressing T-cell specific markers were classified as T-ALL and 33 cases expressing the common ALL antigen (CALLA) as c-ALL. Eighteen of the latter expressed an additional marker, DSA (Daudi surface antigen) splitting c-ALL cases in two subgroups. Cytochemistry of the cases lacking specific surface markers (n = 67) served to diagnose 41 acute myeloid leukemia (AML) cases and 8 monoblastic leukemias. The remaining 18 cases could not be classified. The presence or absence of HLD-DR (Ia) antigens served to subdivide AML into two major subgroups. The prognostic significance of these new diagnostic splits is under active study. (Author abstract) (3 Refs) (In FRE)

43. SURFACE PHENOTYPE OF JAPANESE ADULT T-CELL LEUKEMIA CELLS CHARACTERIZED BY MONOCLONAL ANTIBODIES.

Hattori T, Uchiyama T, Toibana T, Takatsuki K, Uchino H
(c/o Uchiyama) First Div. Internal Medicine, Faculty Medicine, Kyoto Univ., 54 Shogoin-Kawaramachi, Sakyo-ku Kyoto 606, Japan
Blood; 58(3):645-647 1981

We studied the surface phenotype and the functional activities of leukemic cells from three patients with Japanese adult T-cell leukemia (ATL) using the panel of OK and anti-Tac monoclonal antibodies, which react with differentiation antigens and define functionally distinct T-cell subsets or activated and terminally differentiated to T cells. The phenotype of ATL cells were determined to be OKT1+T3+T4+T10+T5-T8-OKla1-, although cells from two patients suppressed pokeweed mitogen (PWM) induced normal B-cell differentiation, and cells from all patients lacked helper activity in this system. In addition, after cultivation with PWM, ATL cells from all patients were reactive with anti-Tac monoclonal antibody, and cells from one patient were reactive with OKlal. These findings suggest that ATL cells arise from peripheral mature T-cell subsets and also suggest that the transition of surface phenotype of ATL cells to functionally mature and activated T cells occurs in culture. (Author abstract) (17 Refs)

44. SPECIFIC RED CELL ADHERENCE TEST AND UNSPECIFIC IMMUNE RESPONSE IN PATIENTS WITH SUPERFICIAL BLADDER CANCER.

Jakse G, Hofstadter F, Mark R
Dept. Urology, Univ. Innsbruck, Anichstrasse 35, A-6020 Innsbruck, Austria
Urol Int; 36(3):171-177 1981

ABH antigenicity and unspecific immune response were evaluated in 31 patients with superficial transitional cell carcinoma. Twenty six percent of these patients showed a reduced dinitrochlorobenzene (DNCB) reaction. There was no significant difference in the monocyte chemotaxis of patients with benign urological diseases and patients with superficial bladder cancer. However, a significant difference exists versus patients with deeply infiltrating carcinomas. Twenty patients revealed a loss of ABH antigens on the initial tumor. During the follow-up of at least 1 yr, patients with negative DNCB skin test, reduced monocyte chemotaxis and negative specific red cell adherence test demonstrated a high rate of recurrent tumors and in one of seven a progressive tumor developed. (Author abstract) (39 Refs)

OTHER RELATED STUDIES

45. ANTIBODIES SPECIFIC FOR THE POLYOMA VIRUS MIDDLE-SIZE TUMOR ANTIGEN.

Walter G, Hutchinson MA, Hunter T, Eckhart W
Institute fur Immunobiologie der Albert-Ludwigs-Universitat, 7800 Freiburg i. Br., W. Germany
Proc Natl Acad Sci USA; 78(8):4882-4886 1981

We have obtained antibodies specific for the polyoma virus middle-size tumor antigen (middle T antigen) by immunizing rabbits with a synthetic peptide, Lys-Arg-Ser-Arg-His-Phe, corresponding to the six carboxy-terminal amino acids of the middle T antigen predicted from the nucleotide sequence of polyoma DNA. The antipeptide serum precipitates the polyoma middle T antigen but not the small or large tumor antigens, and precipitation is inhibited in the presence of the peptide. Two cellular proteins, 30,000 and 26,000 daltons, are also precipitated specifically by the antipeptide serum and may have amino acid sequences related to the peptide. Two other cellular proteins, 33,000 and 25,000 daltons, are precipitated only in the presence of the peptide and may associate with it in cell extracts. Antisera directed against synthetic peptides are likely to be important in various ways, including the production of antibodies directed against particular determinants and the recognition of unknown proteins whose genes have been analyzed. (Author abstract) (21 Refs)

46. A NEW VIEW OF THE ETIOLOGY OF NASOPHARYNGEAL CARCINOMA.

Hirayama T, Ito Y
(c/o Ito) Dept. Microbiology, Faculty Medicine, Kyoto Univ., Kyoto 606, Japan
Prev Med; 10(5):614-622 1981

Epidemiological studies showed a high incidence of nasopharyngeal carcinoma (NPC) in southern regions of China. Also found in these regions are plants of the Euphorbiaceae family, including Croton tiglium (the source of croton oil) and other species used as herbal drugs. Interaction of herbal drugs and anti-Epstein-Barr virus (EBV) titers was noted. Use of the herbal drugs was related to nasal infection by microbes such as Fusobacterium. The combined effects of drug use and EBV induction were synergistic rather than additive. Fusobacteria in culture produced n-butyric acid, which had a low, but definite EBV-inducing activity in human lymphoblastoid P3HR-1 cells. Combined treatment with nanog concentrations of croton oil and n-butyrate produced marked increase in EBV antigens in EBV genome-carrying P3HR-1 and Raji cells. Apparently EBV is induced and activated by the combination of bacterial fatty acid and herbal oils. It is suggested that the activated EBV then initiates steps resulting in NPC. (33 Refs)

47. DETECTION OF ANTIBODIES AND ANTIGENEMIA IN LEUKEMIC PATIENTS WITH CANDIDIASIS BY ENZYME-LINKED IMMUNOSORBENT ASSAY.

Meckstroth KL, Reiss E, Keller JW, Kaufman L

(c/o Reiss) Mycology Div., Centers for Disease Control, Atlanta, GA, 30333

J Infect Dis; 144(1):24-32 1981

Standard tests and two enzyme-linked immunosorbent assays (ELISAs) were compared for detecting systemic candidiasis in 92 leukemic patients. Antibodies to Candida were detected by immunodiffusion (ID), latex agglutination (LA), and indirect ELISA; antigenemia was evaluated by indirect ELISA inhibition. In 48 patients without candidiasis (Group 1), sera from 27% reacted in ID and 13% in LA tests; titers of antibody by ELISA occurred in all patients. In 34 patients without disseminated candidiasis (Groups 2 and 3), Candida species were isolated; sera from 35% and 32% were positive in the ID and the LA test, respectively. In 9 of 10 patients with disseminated candidiasis (Group 4), LA and ID tests were negative. Seven patients in Groups 1-3 without disseminated candidiasis were antigenemic (false-positive rate, 9%). Antigenemia was detected in 7 of 10 patients with disseminated candidiasis; in the remaining three patients sera were drawn too early to be of diagnostic value. Thus, monitoring of immunosuppressed patients for mannan antigenemia is useful for the detection of disseminated candidiasis. (Author abstract) (12 Refs)

48. HODGKIN'S DISEASE: ESTABLISHMENT AND CHARACTERIZATION OF FOUR IN VITRO CELL LINES.

Diehl V, Kirchner HH, Schaadt M, Fonatsch C, Stein H, Gerdes J, Boie C

Dept. Hematology/Oncology, Inst. Genetics, Sch. Medicine, Karl-Wiechert-Allee 9, D-3000 Hannover, W. Germany

J Cancer Res Clin Oncol; 101(1):111-124 1981

Four in vitro cells established from the pleural effusions of two Hodgkin's disease (HD) patients and from the blood and bone marrow of a third were characterized morphologically, immunologically, and biochemically. The malignant nature of the cultured cells was confirmed by the presence of structural and numerical chromosome abnormalities, the monoclonality of marker chromosomes, and the lack of Epstein-Barr virus-specific antigens. The cells gave rise to tumors in nude mice following intracranial transplantation and induced sc tumors when embedded on plasma dots before transplantation. All four lines were positive for Ia-like antigens, T-cell receptors, acid phosphatase, and acid esterase; they were negative for lysozyme peroxidase, chloracetate esterase, surface Ig or cytoplasmic Ig (CIg), and receptors for complement 3b, complement 3d, IgG-FC, and mouse or sheep RBC. Except for the lack of CIg in the in vitro cells, the marker pattern corresponded to that of Hodgkin's and Sternberg-Reed cells in biopsy material. The phenotype was not that of B cells, T cells, myeloid cells, monocytes, or macrophages. (26 Refs)

49. FACTORS STIMULATING AND INHIBITING TUMOR GROWTH IN CARCINOGENESIS.

Kochergina NI, Kosova IP
Res. Lab. Experimental Immunobiology, Moscow, USSR
Usp Sovrem Biol; 91(3):409-418 1981

Literature data on tumor factors that can stimulate or inhibit proliferation of normal or neoplastic cells are reviewed. Factors isolated from murine sarcoma 180, spontaneous and explanted murine mammary gland carcinomas, tissue-specific inhibitors of cell divisions (chalones), and polysomal RNA from Rous sarcoma cells were found to regulate the neoplastic growth and to affect tumor transplantability. Tumor factors were shown to inhibit the antibody formation. The sera of cancer patients was shown to contain factors that inhibited lymphocyte cytotoxicity. In response to stimulation with tumor antigens, T lymphocytes formed the clone of killer cells. The degree of lymphocyte transformation depended upon the ratio of lymphocytes and tumor antigen. Tumor factors were found to inhibit not only the antitumor but also the transplacental immunity. Stimulation of tumor antigenicity can stimulate the immune system of tumor-bearing organism and thus can have an immunotherapeutic effect. (108 Refs) (In RUS)

50. FIBRONECTIN AND RELATED TRANSFORMATION-SENSITIVE CELL SURFACE PROTEINS (ONCOLOGY OVERVIEW).

International Cancer Research Data Bank
ICRDB Program Office, NCI, Westwood Building, Room 10A18, Bethesda, MD, 20205
Fibronectin and Related Transformation-Sensitive Cell Surface Proteins (Oncology Overview) Chen, L B, ed This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-923001:; OB-81/01:95pp. 1981

Oncology Overviews are a service of the International Cancer Research Data Bank (ICRDB) Program of the National Cancer Institute. They are retrospective bibliographies containing 100-500 selected abstracts of published research on topics of high interest to cancer investigators. The scope of this Oncology Overview covers the purification, localization, structure, and function of the 220,000 dalton cell surface transformation-sensitive protein fibronectin (also known as LETS protein, CIg, soluble fibroblast antigen, cell surface protein, and zeta protein). The dramatic reduction of cell surface fibronectin which occurs during transformation may become a useful marker characteristic in correlations of tumorigenicity and the transformed phenotype. The expression of fibronectin on a variety of normal and transformed cells, and the control of expression, are reviewed. Other areas of fibronectin research which are covered include: the influence of mitogenic proteases on fibronectin in relation to cell growth control; fibronectin interactions with collagen and proteoglycan; ultrastructure of intercellular fibronectin matrix; fibronectin's role in cell-cell adhesion, cell-substratum adhesion, cell surface centripetal flow inhibition, cell motility and restoration of cultured cells to normal phenotype; and differentiation-associated alterations in cell surface fibronectin. Also included are studies of the transformation-sensitive cell surface proteins which are relevant to fibronectin research.

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MARCH, 1982

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DETECTION/ CHARACTERIZATION/ ISOLATION

1. ADULT T-CELL LEUKEMIA: ANTIGEN IN AN ATL CELL LINE AND DETECTION OF ANTIBODIES TO THE ANTIGEN IN HUMAN SERA.

Hinuma Y, Nagata K, Hanaoka M, Nakai M, Matsumoto T, Kinoshita KI, Shirakawa S, Miyoshi I
Inst. Virus Res., Kyoto Univ., Kyoto 606, Japan
Proc Natl Acad Sci USA; 78(10):6476-6480 1981

Indirect immunofluorescence of certain human sera demonstrated an antigen(s) in the cytoplasm of 1-5% of the cells of a T-cell line, MT-1, from a patient with adult T-cell leukemia (ATL), which is endemic in southwestern Japan. The antigen was not detected in other human lymphoid cell lines, including six T-cell lines, seven B-cell lines, and four non-T non-B cell lines. The antigen did not show cross antigenicity with that of

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herpesviruses, including Epstein-Barr virus, herpes simplex virus, cytomegalovirus, varicella-zoster virus, herpesvirus saimiri, and Marek disease virus. The proportion of antigen-bearing cells was increased by a factor of approx five on culture in the presence of 5-iodo-2'-deoxyuridine. Antibodies against the antigen in MT-1 cells were found in all 44 patients with ATL examined and in 32 of 40 patients with malignant T-cell lymphomas (most of them had diseases similar to ATL except that leukemic cells were not found in the peripheral blood). The antibodies were also detected in 26% of the healthy adults examined from ATL-endemic areas but in only a few of those examined from ATL-non-endemic areas. On electron microscopy, extracellular Type C virus particles were detected in pelleted MT-1 cells cultured in the presence of 5-iodo-2'-deoxyuridine. (Author abstract) (26 Refs)

2. ACUTE MYELOBLASTIC LEUKEMIA-ASSOCIATED ANTIGENS: DETECTION AND CLINICAL IMPORTANCE.

Baker MA, Roncari DA, Taub RN, Mohanakumar T, Falk JA
No affiliation given
Haematol Blood Transfus; 26:332-337 1981

An analysis of material released into the supernatant medium of cultured myeloblasts of patients with acute myeloblastic leukemia was performed. Leukemia myeloblasts labeled with the lactoperoxidase 125I iodination technique released soluble compounds into the culture media that reacted immunologically with alloantisera to leukemia-associated antigens. Antisera raised in monkeys to compounds eluted from a diethylaminoethanol column were used to raise heteroantisera in monkeys that were selectively reactive with leukemic myeloblasts and unreactive with nonleukemic cells. Further study of compounds eluted from gel columns were applied to isoelectric focusing (pI). Fractions obtained were analyzed for reactivity by coprecipitation with the heteroantisera. Analysis of the immune precipitate of a major reactive peak at pI 7.8 yielded a homogeneous peak with a mol wt between 70,000 and 80,000 daltons. Sera from patients with acute myeloblastic leukemia significantly inhibited the reactivity of the heterosera, suggesting the soluble leukemic antigen is released in vivo as well. (28 Refs)

3. BIOCHEMICAL CHARACTERIZATION OF AN ANTIGEN ASSOCIATED WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND LYMPHOCYTE PRECURSORS.

Newman RA, Sutherland DR, Greaves MF
Imperial Cancer Res. Fund Lab., P.O. Box 123, Lincoln's Inn Field, London WC2A 3 PX, England
Haematol Blood Transfus; 26:326-328 1981

An antigen (ALLA) occurring on the surface membrane of cells from patients with common acute lymphoblastic leukemia (ALL) was previously identified. ALLA was also found in some cases of undifferentiated leukemias and chronic myeloid leukemia and in a small proportion of normal bone marrow cells. ALLA from the cell line Nalm-1 was characterized biochemically. ALLA is a glycosylated polypeptide of approx 100,000 daltons. No intrachain disulfide linkages are present. ALLA shows 50% binding with lentil lectin, but 100% binding with Ricinis communis lectin. Lectin binding and nonbinding forms form identical homogeneous spots in two-dimensional isoelectric focusing with a pI of 5.1-5.5. Neuraminidase treatment of both forms causes a shift of approx 0.6 towards the basic end of the gel. Treatment with tunicamycin and glycosidases indicate that up to 25% of ALLA mol wt may be carbohydrate, but carbohydrate is not involved in the antigenic site. ALLA is apparently not integral to the cell membrane, but is closely associated with it. Presence of ALLA in some normal bone marrow cells suggests the antigen is a normal product reflecting target cells for malignant transformation and/or the stage of maturation arrest of ALL cells. (11 Refs)

4. NEW ANTIGENIC DETERMINANT COMMON TO HUMAN THYMUS LEUKAEMIA-ASSOCIATED ANTIGENS AND COMMON ACUTE LYMPHOBLASTIC LEUKAEMIA ANTIGEN.

Negoro S, Yoshizaki K, Henderson ES, Seon BK
(c/o Seon) Dept. Immunology Res., Roswell Park Memorial Inst., Buffalo, NY, 14263
Clin Exp Immunol; 45(3):487-495 1981

In the present paper we demonstrate that there is an antigenic determinant common to two different types of human leukemia-associated antigens, ie human thymus leukemia-associated (HTL) antigens and common acute lymphoblastic leukemia (cALL) antigen. In addition, there are distinct antigenic determinants which are unique to the HTL antigens or to the cALL antigen. The new, common antigenic determinant will be useful as a new differentiation marker of human hematopoietic cells as well as a new leukemia-associated marker. In the present study, we used several different anti-human leukemia antisera which include those prepared by immunizing rabbits (Numbers 7549 and 7550) with purified HTL antigens. The antisera 7549 and 7550, without any absorption, showed strong specificity as well as strong antibody activity toward leukemia cells. These are the first anti-human leukemia antisera, except for the monoclonal hybridoma antibodies, that show good specificity for leukemia cells without prior absorption. (Author abstract) (33 Refs)

5. DISTRIBUTION OF COMMON ACUTE LYMPHOBLASTIC LEUKEMIA ANTIGEN IN NONHEMATOPOIETIC TISSUES.

Metzgar RS, Borowitz MJ, Jones NH, Dowell BL
Dept. Microbiology, Duke Univ. Medical Center, Durham, NC, 27710
J Exp Med; 154(4):1249-1254 1981

The presence of common acute lymphoblastic leukemia antigen (CALLA) in certain cell types of nonhematopoietic adult and fetal tissues was examined by immunoperoxidase staining with the J-5 monoclonal antibody. Portions of normal tissues were removed during the course of surgery from patients with l eukemia or lymphoma and a 20-wk-old fetus was obtained from a prostaglandin-induced abortion. Compared to control ascites fluid from BALB/c mice injected ip with the P3 x 63Ag8 myeloma cell line (P3), no significant staining was found in the fetal heart, liver, lung, pancreas, salivary gland, spleen, or thymus, or in the adult skeletal muscle, spleen, tonsil, salivary gland, small intestine, or colon. However, significant staining was observed in adult kidney, fetal kidney, fetal small intestine, and the myoepithelial cell layer of adult breast. In particular, the J-5 antigen was present on proximal tubules and glomeruli of the kidney. The glomerular staining may have been on the podocyte and not the basement membrane. CALLA was shown to migrate as a 90,000 mol wt antigen rather than the 98,000-100,000 mol wt antigen noted on CALLA-positive tissue culture cell lines. The determinant defined by the J-5 monoclonal antibody may be neither lymphoid cell-specific differentiation antigen nor leukemia-specific antigen. (20 Refs)

6. HUMAN LIVER NUCLEOLAR ANTIGENS.

Busch RK, Busch H
Dept. Pharmacology, Baylor Coll. Medicine, Houston, TX, 77030
Proc Soc Exp Biol Med; 168(1):125-130 1981

Normal human liver nucleoli were used to immunize rabbits and the resultant antibodies were used to study antigens in human liver and other tissues. Immunofluorescence studies with the antibodies to human liver nucleoli, showed nucleoli as bright fluorescent organelles against a less fluorescent nuclear background. In most tissue sections, a limited number of fluorescent nucleoli were observed. Nuclear membrane fluorescence was frequently observed. In HeLa cells, the localization of fluorescence was less restricted. Nucleolonemal and nuclear network fluorescence was visible. In the placental sections, few nucleoli were found and more background fluorescence was noted. Immunodiffusion analysis revealed two immunoprecipitin bands which appeared to be liver specific. Other immunoprecipitin bands were common to liver, placenta, and HeLa nuclear extracts. Rocket immunoelectrophoresis revealed two liver-specific antigens (L1 and L4), one migrating to the cathode and the other to the anode. Thus liver nucleolar-specific antigens, not found in Hela placental cells, were identified. It was suggested that since a neoplasm may result from a loss of normal protein, information on normal human liver nucleolar and nuclear antigens may aid in the detection of specific proteins lost in neoplasia. (16 Refs)

7. MONOCLONAL ANTIBODIES TO DIFFERENTIATION ANTIGENS OF NORMAL HUMAN MAMMARY EPITHELIAL CELLS (MEETING ABSTRACT).

Peterson JA, Moncada FR, Ceriani RL
Bruce Lyon Memorial Research Laboratory, Children's Hospital Medical, Center 51st and Grove Streets, Oakland, CA, 94609
In Vitro; 17(3):225 1981

Hybridomas were prepared that secrete monoclonal antibodies to surface antigens of normal human mammary epithelial (HME) cells by fusion of mouse myeloma cells with spleen cells from BALB/c mice immunized with human milk fat globule (HMFG) membranes. Preliminary selection for presumptive breast specificity was based on specific binding to HMFG membranes and not to membranes from human mammary fibroblasts, or HeLa, HT-29, or lymphoblastic cell lines. Specificity of binding to HME cells was shown by competion with solubilized HMFG and with rabbit anti-HME antisera. Five different hybridomas have been prepared, all of which bind to surface antigens of normal HME cells while each binds differently to several human breast carcinoma cell lines, thus indicating a heterogeneity in surface antigens of breast tumors. We have previously shown that the HMFG membrane is made up of four major components, three of which contain antigens specific for HME cells. The monoclonal antibodies bind to at least two different mol wt components. These hybridomas will be useful in characterizing surface antigens of normal HME cells and in classifying breast tumors. (1 Ref)

8. IMMUNOCHEMICAL REACTIVITY OF SIMIAN SARCOMA VIRUS POLYPEPTIDES ISOLATED BY PREPARATIVE SODIUM DODECYL SULFATE POLYACRYLAMIDE GEL ELECTROPHORESIS.

Johnson JC, Higuchi T, Geissler E
Dept. Biological Sciences, Old Dominion Univ., Norfolk, VA, 23508
Can J Microbiol; 27(2):238-242 1981

The polypeptides associated with a zonal centrifugation purified simian sarcoma virus propagated in lymphoblastoid NC-37 cells were isolated by preparative polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulfate (SDS) using a procedure designed to minimize the loss of immunochemical reactivity. The proteins p10, p15, p28, p36, p44, p75, and p86 were obtained in large yield and high degree of homogeneity. The electrophoretically purified p28 was analyzed by competition radioimmunoassay using antiserum to a pore exclusion and ion exchange purified simian sarcoma virus p28. Complete competition was observed with extracts of simian sarcoma virus infected cells. No competition was observed with uninfected or unrelated, infected cell extracts. The antigen-antibody affinity as measured by the slope of the competition curve using antiserum to p28 and 125I-labeled and electrophoretically purified p28 was the same as that for the p28 released from sonication-disrupted simian sarcoma virus. The data indicates that preparative purifications by polyacrylamide gel electrophoresis in the presence of SDS may be generally applicable for the isolation of proteins with essentially the same immunospecificities and affinity for a specific antiserum as proteins isolated by procedures that avoid the use of SDS and electrophoresis. (Author abstract) (21 Refs)

IMMUNOLOGICAL STUDIES

9. ENHANCEMENT OF CYTOTOXICITY OF HUMAN PERIPHERAL BLOOD LYMPHOCYTES BY INTERFERON.

Kato T, Minagawa T
Dept. Microbiology, Hokkaido Univ. Sch. Medicine, Kita-ku, Sapporo, Hokkaido 060, Japan
Microbiol Immunol; 25(8):837-845 1981

The usefulness of the human lung carcinoma cell line (Pc-10) and Pc-10 cells persistently infected with mumps virus (Pc-10/MpV) as target cells for analyzing the relationship between alpha-interferon (IFN-alpha) and human natural killer (NK) activity was examined. Both Pc-10 and Pc-10/MpV were found to be useful as target cells. Pc-10/MpV were lysed more efficiently that uninfected Pc-10 cells by the same lymphocyte subpopulation, namely non-T, non-B cells, which correspond in part to NK cells. Human peripheral blood mononuclear leukocytes (PBML) were obtained from healthy donors who had antibody against mumps virus in their blood and were sensitive to mumps virus antigens in the skin reaction; no T cell-dependent cytotoxicity for Pc-10/MpV cells was observed. NK activity and the production of IFN/alpha in human PBML could not be dissociated, since anti-IFN-alpha suppressed the NK activity of PBML. Augmentation of the cytotoxicity of PBML by IFN-alpha was detectable within 2 hr of incubation. The effect of IFN-alpha on the augmentation of the cytotoxicity of human PBML for Pc-10 was dependent on the dose from 0.8-60 IU/ml. No difference between the augmentation of the cytotoxicity of human PBML by gamma-interferon and IFN/alpha was observed. (39 Refs)

10. GRANULOPOIETIC DIFFERENTIATION IN AML BLASTS IN CULTURE.

Marie JP, Izaguirre CA, Civin CI, Mirro J, McCulloch EA
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Blood; 58(4):670-674 1981

A newly described monoclonal antibody detected an antigen (My-1) that is expressed on the cell surface during normal granulopoietic differentiation. The kinetics of expression of My-1 and NASD chloracetate esterase were studied during the formation in culture of blast colonies and normal granulopoietic colonies. My-1-positive cells increased during blast colony formation in six of nine experiements, while NASD esterase-positive cells decreased. In contrast, in normal granulopoiesis in culture both markers increased coherently. We suggest that components of granulopoietic differentiation programs are expressed abnormally during blast colony formation in culture. (Author abstract) (19 Refs)

11. USE OF MONOCLONAL ANTIBODIES AS DIAGNOSTIC AND THERAPEUTIC REAGENTS IN ACUTE LYMPHOBLASTIC LEUKEMIA.

Ritz J, Pesando JM, Notis-McConarty J, Clavell LA, Sallan SE, Schlossman SF
Div. Tumor Immunology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115
Cancer Res; 41(11,part2):4771-4775 1981

A monoclonal antibody specific for a common acute lymphoblastic leukemia (ALL) a ntigen has been generated and characterized. This antibody (J-5) is reactive with leukemic cells from most patients with non-T-cell ALL and some patients with chronic myelocytic leukemia in blast crisis. J-5 antibody is not reactive with leukemic cells from patients with either T-cell ALL, chronic lymphocytic leukemia, acute myeloblastic leukemia, or stable-phase chronic myelocytic leukemia. In addition to diagnostic applications, anti-common ALL antigen monoclonal antibody has been used to study the effect of specific serotherapy in the treatment of ALL. In the first patient with ALL treated with J-5 antibody, a 90% reduction in circulating lymphoblasts occurred within 1 hr of starting antibody infusion. Despite continued serotherapy, however, lymphoblasts persisted in peripheral blood and bone marrow. Analysis of cell surface markers during serotherapy suggested that resistance to antibody-mediated lysis in vivo may have been due to antigenic modulation of leukemic cells in response to J-5 monoclonal antibody. (Author abstract) (27 Refs)

12. EXPRESSION OF MYELOID DIFFERENTIATION ANTIGENS ON NORMAL AND MALIGNANT MYELOID CELLS.

Griffin JD, Ritz J, Nadler LM, Schlossman SF
Div. Tumor Immunology, Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA, 02115
J Clin Invest; 68(4):932-941 1981

A series of monoclonal antibodies have been characterized that define four surface antigens (MY3, MY4, MY7, and MY8) of human myeloid cells. They were derived from a fusion of the NS-1 plasmacytoma cell line with splenocytes from a mouse immunized with human acute myelomonocytic leukemia cells. MY3 and MY4 are expressed by normal monocytes and by greater than 90% of patients with acute monocytic leukemia or acute myelomonocytic leukemia, but are detected much less often on other types of myeloid leukemia. MY7 is expressed by granulocytes, monocytes, and 5% of normal bone marrow cells. Seventy nine percent of all acute myeloblastic leukemia (AML) patients tested (72 patients) express MY7 without preferential expression by any AML subtype. MY8 is expressed by normal monocytes, granulocytes, all peroxidase-positive bone marrow cells, and 50% of AML patients. MY3, MY4, and MY8 define myeloid differentiation antigens in that they are not detected on myeloid precursor cells and appear at discrete stages of differentiation. These antigens are not expressed by lymphocytes, RBC, platelets, or lymphoid malignancies. The monoclonal antisera defining these antigens have been used to study differentiation of normal myeloid cells and malignant myeloid cell lines. (Author abstract) (49 Refs)

13. EXPRESSION OF COMMON ACUTE LYMPHOBLASTIC LEUKAEMIA ANTIGEN AND TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE IN NORMAL MONONUCLEAR BLOOD CELLS DURING DIFFUSION CHAMBER CULTURE.

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Scand J Haematol; 27(1):5-8 1981

Peripheral mononuclear blood cells of two healthy individuals were cultured over a 13 day period in diffusion chambers. A high percentage of cALL antigen positive cells and later on TdT containing cells appeared during culture. The cALL+ cells could be clearly distinguished into two groups: a population with weak and diffuse fluorescence and a small number of ring-like brightly dyed cells. The first group develops into TdT+ cells and therefore resembles immature T-cells. The interpretation of the ring-like stained cells is still preliminary, but it cannot be excluded, that these cells represent a cell population with more than lymphatic differentiation capacity. (Author abstract) (12 Refs)

14. TERMINAL DIFFERENTIATION SURFACE ANTIGENS OF MYELOMONOCYTIC CELLS ARE EXPRESSED IN HUMAN PROMYELOCYTIC LEUKEMIA CELLS (HL60) TREATED WITH CHEMICAL INDUCERS.

Perussia B, Lebman D, Ip S H, Rovera G, Trinchieri G
Wistar Inst. Anatomy and Biology, 36th and Spruce St., Philadelphia, PA, 19104
Blood; 58(4):836-843 1981

The expression of two surface antigens present on the cell membrane of both human granulocytes and monocytes was studied during the process of myelomonocytic differentiation using two monoclonal antibodies (B9.8.1 and B13.4.1). These surface antigens are not present on immature myeloid cells nor on nonmyeloid hematopoietic cells, but can be detected when the cells are terminally differentiated. Among the bone marrow cells, B13.4.1 binds to metamyelocytes and B9.8.1 to metamyelocytes and a fraction (30%) of myelocytes. HL60 human promyelocytic leukemia cells did not react with such monoclonal antibodies. However, when such cells were induced to differentiate in vitro into mature myeloid elements by treatment with retinoic acid or dimethyl sulfoxide, 70%-90% of the differentiated cells expressed both surface antigens. Cell sorting studies on these treated HL60 cells indicated that myelocytes and metamyelocytes were the most immature cells expressing such markers. Expression of the two surface antigens was also observed when HL60 cells were induced to differentiate into monocyte/macrophage cells by treatment with the tumor promoter 12-0-tetradecanoyl-phorbol-13-acetate. Thus, human promyelocytic leukemia cells induced to differentiate in vitro by treatment with specific chemical agents express membrane antigens in the same pattern as normal bone marrow myeloid cells at the corresponding stage of differentiation. (Author abstract) (26 Refs)

15. EXPRESSION OF TUMOR-ASSOCIATED ANTIGENS AND KINETIC PROFILE OF TWO IN VITRO HUMAN MELANOMA CELL LINES.

Badaracco G, Corsi A, Maisto A, Natali PG, Starace G, Zupi G
Istituto Regina Elena per lo Studio e la Cura dei Tumori, Rome, Italy
Cytometry; 2(2):63-69 1981

The growth characteristics and the antigenic profile of established human melanoma cell lines M10 and M14 are reported. While growth curves in culture, studied by flow cytometry, were fairly typical, there were some unusual features which were confirmed by their DNA distribution content. In the late stages of growth the cell DNA content resumes the initial distribution, suggestive of partial recovery of cell proliferating potential. Reactivity of three monoclonal antibodies (MoAb) to human melanoma associated antigens was assessed in normal and transformed melanocytes by indirect immunofluorescence (IIF). Staining of M10 and M14 lines with the three MoAb 225, 465 and Q5/13 showed that expression of melanoma-associated antigens as detected by IIF on the plasma membranes did not exhibit appreciable variations during the different growth phases studied during 4-13 days of culture. (9 Refs)

16. SELF AND NON-SELF IN THE BRAIN.

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Immunol Today; 2(9):176-184 1981

Relationships between the immune system, the brain, and developing malignant gliomas are reviewed. Specific subjects discussed are the structure and function of the blood-brain barrier (BBR), experimental and clinical evidence for an immunologically effective BBR, the 'leakiness' of blood vessels in brain tumors, extent of brain tolerance to tumor or skin grafts, possible immune reactions to gliomas (tumor antigenicity, shedding of brain antigens into serum or cerebrospinal fluid, macrophage levels in tumors),and in vitro studies of immunity in glioma patients. Available evidence suggests that brain antigens may pass through the BBR in glioma patients to induce cell-mediated and humoral responses. In some patients, the antigens may form circulating immune complexes that inhibit immune responses. (43 Refs)

17. MECHANISM OF ACTION OF BCG-TUMOR CELL VACCINES IN THE GENERATION OF SYSTEMIC TUMOR IMMUNITY. I. SYNERGISM BETWEEN BCG AND LINE 10 TUMOR CELLS IN THE INDUCTION OF AN INFLAMMATORY RESPONSE.

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JNCI; 67(4):853-861 1981

The id injection of a vaccine composed of 10(7) X-irradiated, syngeneic hepatocarcinoma line 10 (L10) cells admixed with 10(8) Mycobacterium bovis strain BCG into inbred Sewall Wright Strain 2 guinea pigs induced a local acute and then chronic inflammatory response. Cellular analysis of enzymatically dispersed dermal vaccination sites and regional lymph nodes revealed quantitative differences between the cellular infiltrate induced by a mixed BCG-tumor cell vaccine and the inflammation induced by either 10(8) BCG alone or 10(7) tumor cells alone. Analysis of dermal sites from Days 1 through 4 following vaccination showed that sites receiving the BCG-tumor cell vaccine contained twofold to fourfold more cells than did those induced by BCG alone and more than fourfold the number of cells induced by L10 cells alone. These results indicated that there was a synergistic interaction between BCG and L10 cells in the induction of an inflammatory response at the site of vaccination. Analysis of the superficial distal axillary lymph nodes draining the site of vaccination revealed a similar synergistic interaction between BCG and L10, such that lymph nodes draining vaccination sites had a greater total cellular content than that induced by either BCG or L10 cells administered separately. When two other tumors, also syngeneic to Strain 2 guinea pigs, were tested for their ability to interact synergistically with BCG to elicit an inflammatory response, it was found that the antigenically distinct hepatocarcinoma Line 1 tumor also shared this characteristic with L10, wheres the L2C B-cell leukemia did not. (Author abstract) (36 Refs)

18. PHOSPHOFRUCTOKINASE ISOZYMES OF MORRIS HEPATOMAS.

Dunaway GA, Naqui D, Kruep D, Thrasher JR, Morris HP
Dept. Pharmacology, Sch. Medicine, Southern Illinois Univ., Springfield, IL, 62708
Arch Biochem Biophys; 212(1):1-8 1981

Phosphofructokinase (PFK) from Morris hepatoma was analyzed using agarose gel electrophoresis, DEAE-cellulose chromatography, and immunological titration with fast migrating hepatic isozyme (PFK-L2) and muscle type PFK (PFK-M) specific antiserums. Separation of PFK isozymes by agarose gel electrophoresis revealed one PFK isozyme in muscle and two in liver (PFK-L2 and slower migrating liver isozyme (PFK-L1)). Morris hepatoma isozymes were designated as PFK-1, PFK-2, and PFK-3 in order of their elution from DEAE-cellulose. It was found that PFK-L2 and PFK-3 had similar affinities for DEAE-cellulose and that PFK-1 had similar elution profiles with both PFK-L1 and PFK-M which have the same electrophoretic mobility. Also, PFK-2 was observed to have an elution pattern intermediate between PFK-L2 and PFK-L1 or PFK-M. Incubation of supernatant fluid from adult muscle with PFK-L2 antiserum did not result in a measurable loss of PFK activity. However, the PFK activity in supernatant fluids from liver, as well as poor, well, and highly differentiated hepatomas was diminished significantly when incubated with this antiserum. Treatment of supernatant fluid prepared from hepatoma 3924A with PFK-L2 antiserum resulted in a loss of the PFK-L2 isozyme and the PFK-H isozyme. The results indicated that in Morris hepatomas, regardless of their differentiation state there are at least three PFK isozymes, PFK-L2, PFK-M, and PFK-H. These data suggested that PFK-H, which is present in highest concentration in the poorly differentiated hepatomas, exhibits antigenic determinants common with PFK-L2 and PFK-M. (18 Refs)

19. EPOXIDE HYDROLASE AND HEPATOCARCINOGENESIS.

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Trends Pharmacol Sci; 2(10):257-258 1981

The role of epoxide hydrolase (EH) in hepatocarcinogenesis is described. A search for markers associated with multistage development of preneoplastic cells through focal and nodular stages to a hepatoma led to the discovery of the preneoplastic (PN) antigen, a microsomal antigen present in nodule and hepatoma cells. Through immunological studies EH was found to be a major PN antigen. A class of heterocyclics, including isoquinoline, norharman, and ellipticine, has been shown to stimulate microsomal EH. The requirement for a pyridinic nitrogen beta to a ring fusion suggests enzyme dictated specificity, while the pyridinic nitrogen suggests an electrophilic target. Reactive electrophiles, such as epoxides, have been found to regulate cell function and development. Perhaps endogenously formed epoxides play a role in liver adaptation during hepatocarcinogenesis. All hepatocarcinogen tests seem to cause an early (1-5 wk) induction of EH activity and microsomal content of the enzyme protein. One explanation for this early induction of EH is the production of increased amounts of an endogenous epoxide as an acute response. EH regulation during hepatocarcinogenesis is discussed with 2-acetylaminofluorene hepatocarcinogenesis as an example. (12 Refs)

20. RECEPTOR MEDIATED MURINE LEUKEMOGENESIS: MONOCLONAL ANTIBODY INDUCED LYMPHOMA CELL GROWTH ARREST.

McGrath MS, Jerabek L, Pillemer E, Steinberg RA, Weissman II.

Dept. Pathology, Stanford Univ. Medical Center, Stanford, CA, 94305

Haematol Blood Transfus; 26:360-364 1981

A receptor-mediated leukemogenesis hypothesis that T lymphocytes are clones of T cells bearing mitogen-linked surface receptors specific for the envelope determinants of the inducing murine leukemia virus was tested. Experiments examined the central postulate that continued leukemic proliferation is the result of continued antigenic stimulation of T lymphomas. Monbclonal antibody reagents to leukemia cell surface determinants were raised; the effect of these antibodies was tested on leukemic cell proliferation in vitro and on specific virus binding to the cells. Several antibodies which inhibited lymphoma cell proliferation in vitro were found. Evidence is presented that inhibition may be due to a blockade in virus binding to these cells. (17 Refs)

21. INHIBITION OF ANTIGEN-INDUCED T-CELL PROLIFERATION BY ANTIBODIES TO ENDOGENOUS AKR-MULV.

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Cell Immunol; 64(1):102-118 1981

Lymph node cells from BALB/c mice immunized with ovalbumin or human gamma-globulin were restimulated in vitro with these antigens and assayed for antigen-induced proliferation. The proliferative response was shown to be antigen specific and T cell dependent. A rabbit antiserum to envelope and core proteins of AKR murine leukemia virus was found to inhibit antigen-induced T-cell proliferation. The IgG fraction and F(ab')2 fragments of the antiserum were also inhibitory. The inhibition occurred after the initial step of antigen-T cell interaction and viral absorption studies showed the inhibition to be specific for anti-AKR virus antibodies. A hypothesis for the mechanism of inhibition is discussed in relation to a functional role for endogenous murine leukemia virus. (Author abstract) (36 Refs)

VIRUS ASSOCIATED ANTIGENS

22. SUMMARY: SYMPOSIUM ON EPSTEIN-BARR VIRUS-INDUCED LYMPHOPROLIFERATIVE DISEASES IN IMMUNODEFICIENT PATIENTS.

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Cancer Res; 41(11,part1):4302-4304 1981

The possibility that the X-linked lymphoproliferative syndrome, renal transplant lymphomas, and other lymphomas in immunodeficient patients originate in proliferating Epstein-Barr virus (EBV)-carrying lymphoid cells is discussed. Evidence for this association included the detection of EBV nuclear antigen (EBNA) in virus-transformed cells and changes in EBV antibody titers in immunodeficiency conditions. Defects of the T-cell system were associated with increased titers against EBV early and viral capsid antigens and decreased anti-EBNA titers. Chronic infectious mononucleosis patients and X-linked lymphoproliferative syndrome patients showed marked impairment of all effector mechanisms involved in the rejection of EBV-carrying cells. (23 Refs)

23. ACYCLOVIR TREATMENT OF EPSTEIN-BARR VIRUS (EBV) INDUCED POST-TRANSPLANT LYMPHOMA (MEETING ABSTRACT).

Hanto DW, Sakamoto K, Purtilo D, Balfour HH, Simmons RL, Najarian JS

University of Minnesota, Minneapolis, MN, 55455

Program and Abstracts of the 21st Interscience Conference on Antimicrobial Agents and Chemotherapy, November 4-6, 1981, Chicago, Illinois American Society for Microbiology; :A30 1981

Lymphoma occurs in 0.7% of renal transplant recipients and the mortality is high (90%). No effective therapy has been reported. Acyclovir (ACV) an anti-viral agent, has promise to this application in light of our evidence that EBV is the cause of these tumors. A transplant developed a tumor in lymph nodes, tonsils, and bone marrow. Cell markers showed a B cell proliferation producing Ig of polyclonal specificity (IgM, IgG, and IgG, kappa and lambda). Staining for EBV nuclear antigen was positive and cyclic RNA/DNA filter hybridization demonstrated 3 EBV genome equivalents per tumor cell. Oropharyngeal shedding of EBV was shown. ACV for 7 days resulted in a dramatic objective and subjective response; EBV shedding disappeared. Forty-eight hr after stopping ACV, fever, symptoms, and objective tumor growth recurred. A second ACV course resulted in resolution lasting 3 mo. A polyclonal B cell recurrence responded to ACV. One mo later a third recurrence, resistant to ACV, resulted in patient death. Cell markers demonstrated sIg/cIg of the IgG kappa class only. ACV is effective during the polyclonal growth phase of these EBV induced lymphomas. The tumor probably evolved into a monoclonal neoplasm which was resistant to ACV. This is the first documented in vivo effect of ACV on EBV. (no Refs)

24. SEROEPIDEMIOLOGIC STUDIES IN HODGKIN'S DISEASE.

Kokosha LV, Lapin BA, Lebedev VN, Danilova NV, Arshba NN, Bologov VN
Lab. Experimental Oncology, Inst. Experimental Pathology and Therapy, Sukhumi, USSR
Probl Gematol Pereliv Krovi; 26(8):12-16 1981

To evaluate the possibility of horizontal transmission of Epstein-Barr virus (EBV), antibodies against capsid antigen of EBV were determined in 109 patients with Hodgkin's disease (HD) and in 67 relatives of 46 patients. High titers of antivirus antibodies were recorded in 70% of the patients with HD. The highest titers were recorded in the patients with lymphoid exhaustion (1:256, compared with 1:97 in lymphoid predominance and mixed cell variant, and 1:49 in nodular sclerosis). The titers of antibodies against EBV antigen in the relatives were significantly greater that that in healthy donors (1:69 and 1:6, respectively). (34 Refs) (In RUS)

25. DOCUMENTATION OF EPSTEIN-BARR VIRUS INFECTION IN IMMUNODEFICIENT PATIENTS WITH LIFE-THREATENING LYMPHOPROLIFERATIVE DISEASES BY CLINICAL, VIROLOGICAL, AND IMMUNOPATHOLOGICAL STUDIES.

Purtilo DT, Sakamoto K, Saemundsen AK, Sullivan JL, Synnerholm AC, Anvret M, Pritchard J, Sloper C, Sieff C, Pincott J, Pachman L, Rich K, Cruzi F, Cornet JA, Collins R, Barnes N, Knight J, Sandstedt B, Klein G
Dept. Pathology Lab. Medicine, Univ. Nebraska Medical Center, 42nd and Dewey Ave., Omaha, NE, 68105
Cancer Res; 41(11,part1):4226-4236 1981

Multiple methods, pedigree analysis, clinical evaluation, and Epstein-Barr virus (EBV)-specific serology, EBV DNA hybridization of tissues to probe for viral genome, staining of touch imprints for EBV nuclear-associated antigen, establishment of spontaneous infected B-cell lines from peripheral blood or tissues, examination of peripheral blood smears, and hematopathology studies, were used to study seven patients with the X-linked lymphoproliferative syndrome and seven additional patients with life-threatening EBV-associated diseases. These studies demonstrated EBV in the tissues of all 14 patients and immunodeficient antibody responses to EBV were documented. This virus can produce various life-threatening lymphoproliferative diseases in a variety of immunodeficient patients. (Author abstract) (35 Refs)

26. EPSTEIN-BARR VIRUS IN A MALIGNANT LYMPHOPROLIFERATIVE DISORDER OF B-CELLS OCCURRING AFTER THYMIC EPITHELIAL TRANSPLANTATION FOR COMBINED IMMUNODEFICIENCY.

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Cancer Res; 41(11,part1):4243-4247 1981

A fatal disseminated polyclonal malignant lymphoproliferative disorder of B-cells (immunoblastic sarcoma) developed shortly after a second thymic epithelial peritoneal implant in a 5-yr-old girl with combined immunodeficiency. The immunodeficiency was characterized by low T-cell numbers and function, very low levels of thymic hormone, dysgammaglobulinemia, and an inability to mount a primary antibody or cell-mediated response to new antigens. At necropsy, the thymus fulfilled morphological criteria for thymic dysplasia. Epstein-Barr virus (EBV) antigen and DNA were identified in neoplastic infiltrates in the lymph nodes and thymus by immunofluorescence for the EBV nuclear antigen and by EBV-specific complementary RNA/DNA hybridization. No antibodies to nuclear antigen, early antigen, or viral capsid antigen of EBV were identified in the serum. The concurrence of these events suggests that the thymic epithelial implant itself may have been instrumental in the pathogenesis of this neoplasm. It is proposed that the thymus may have provided factors which indirectly potentiated the proliferation of EBV-infected B-cells, possibly by induction of nonspecific T-helper cells and perhaps through other thymic humoral factors. It is suggested that some forms of immunoblastic sarcoma, even when polyclonal, and especially those which arise in immunocompromised hosts, may, in some instances, represent an opportunistic form of EBV-induced B-cell neoplasia. (Author abstract) (39 Refs)

27. CLINICAL SPECTRUM OF LYMPHOPROLIFERATIVE DISORDERS IN RENAL TRANSPLANT RECIPIENTS AND EVIDENCE FOR THE ROLE OF EPSTEIN-BARR VIRUS.

Hanto DW, Frizzera G, Purtilo DT, Sakamoto K, Sullivan JL, Saemundsen AK, Klein G, Simmons RL, Najarian JS

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Cancer Res; 41(11,part1):4253-4261 1981

Six renal transplant recipients with abnormal lymphoproliferative disorders were studied in an attempt to define their clinical features and the role of Epstein-Barr virus (EBV) in their pathogenesis. Patients were either teenage (3) or in the sixth decade (3). The younger patients presented an av of 3 mo after transplantation with fever, sore throat, and lymphadenopathy; had been markedly immunosuppressed; frequently had preceding or concomitant cytomegalovirus infections; and two of three had a rapidly fatal course. The older patients presented an av of 5 yr after transplantation while on maintenance immunosuppressive drugs; in two of three cases with an oropharyngeal tumor; and had a more indolent, but frequently fatal, clinical course. The most frequent sites of biopsy-proven involvement in these patients were lymph nodes (3), the oropharynx (3), liver (3), bone marrow (3), transplanted kidney (3), colon (2), and central nervous system (2). EBV-specific antibody titers including anti-viral capsid antigen IgG, anti-viral capsid antigen IgM, anti-early antigen, and anti-Epstein-Barr nuclear antigen were serially measured in all patients. Four patients demonstrated serological evidence of a primary (1) or reactivation (3) EBV infection. No patient had significant changes in anti-early antigen or anti-Epstein-Barr nuclear antigen titers. All three patients tested for oropharyngeal shedding of EBV were positive. A touch imprint of one tumor was stained for the presence of Epstein-Barr nuclear antigen, and a majority of cells were positive. EBV complementary RNA/DNA filter hybridization and/or viral DNA/DNA reassociation analysis performed on tumor biopsy specimens in five patients demonstrated multiple EBV genome equivalents per cell in all eight specimens tested. Clinical, pathological, serological, and molecular hybridization studies provide substantial evidence that EBV was the cause of these lymphoproliferative disorders occurring after renal transplantation. Impaired host defenses allow the EBV-transformed B-lymphocytes to escape normal control mechanisms. This impairment is variable and influenced by many factors resulting in the observed spectrum of disease. Cytogenetic changes, however, may also be important. (Author abstract) (45 Refs)

28. CELL-MEDIATED IMMUNE REACTIONS IN THREE PATIENTS WITH MALIGNANT LYMPHOPROLIFERATIVE DISEASES IN REMISSION AND ABNORMALLY HIGH EPSTEIN-BARR VIRUS ANTIBODY TITERS.

Masucci MG, Szigeti R, Ernberg I, Bjorkholm M, Mellstedt H, Henle G, Henle W, Pearson G, Masucci G, Svedmyr E, Johansson B, Klein G

Dept. Tumor Biology, Karolinska Institutet, S 104 01 Stockholm 60, Sweden

Cancer Res; 41(11,part1):4292-4301 1981

Two patients with Hodgkin's disease in remission and one chronic lymphatic leukemia patient with extraordinarily high anti-Epstein-Barr virus (EBV) (viral capsid antigen) antibody titers (greater than 10,000) were selected to study a spectrum of cell-mediated immune responses, including natural killer, interferon-boosted killer, antibody-dependent lymphocytotoxicity, and T-cell-mediated reactions. The purpose was to compare these reactions in patients with immunosuppression and a high EBV load who can hold their EBV-carrying cells under control with the corresponding reactions in patients with EBV-carrying lymphoproliferative disease. In contrast to the latter group, the three patients of the present study showed a less profound and less general suppression of the immune responses. Multiple effector mechanisms probably safeguard against the proliferation of EBV-transformed B-cells. Clinically manifest EBV-carrying lymphoproliferative disease occurs only in very severe immunodeficiencies effecting multiple effectors. (Author abstract) (44 Refs)

29. CELLULAR IMMUNE DEFECTS TO EPSTEIN-BARR VIRUS-DETERMINED ANTIGENS IN YOUNG MALES.

Masucci MG, Szigeti R, Ernberg I, Masucci G, Klein G, Chessels J, Sieff C, Lie S, Glomstein A, Businco L, Henle W, Henle G, Pearson G, Sakamoto K, Purtilo DT

Dept. Tumor Biology, Karolinska Inst., S 104 01 Stockholm 60, Sweden

Cancer Res; 41(11,part1):4284-4291 1981

Three males with the X-linked lymphoproliferative syndrome (XLP) with hypo- or agammaglobulinemia following Epstein-Barr virus (EBV) infection and two males with the chronic mononucleosis syndrome were investigated for immune responses to EBV-determined antigens. Males with XLP showed profound cellular immune defects. Markedly diminished responses of natural killer cell and interferon-activated killer cell activities and impaired WBC migration inhibition responses to phytohemagglutinin were determined in patients with XLP. The two patients with chronic mononucleosis showed less severe defects. All patients showed partial or complete impairment of their EBV-specific immune responses as measured by WBC migration inhibition. EBV-specific antibodies were markedly diminished against EBV-associated nuclear antigen, early antigen, and viral capsid antigen in males with XLP. In contrast, patients with chronic mononucleosis had elevated antibodies to most EBV-specific antigens. Individuals with life-threatening EBV-induced lymphoproliferative disorders may exhibit multiple defective immune mechanisms against the virus. (Author abstract) (44 Refs)

30. EPISOMAL SIMIAN VIRUS 40 GENOMES IN HUMAN BRAIN TUMORS.

Krieg P, Amtmann E, Jonas D, Fischer H, Zang K, Sauer G

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Proc Natl Acad Sci USA; 78(10):6446-6450 1981

Eight out of 35 human intracranial tumors were shown by restriction enzyme analysis to contain unintegrated simian virus 40 (SV40) DNA molecules. The relative amount of viral DNA was estimated to be the equivalent of one viral genome within every 10th to 20th cell. No infectious virus was detected in tissue cultures established from the tumors. From only one tumor was it possible to rescue, by cell fusion, infectious SV40 displaying wild-type properties. In those cases that permitted a more detailed analysis, the restriction enzyme cleavage patterns appeared to correspond to the wild-type patterns with one exception, in which the SV40 episomes displayed a deletion of approx 70 base pairs close to the origin of DNA replication. From one tumor, the SV40 genomes were transferred into permissive CV-1 monkey cells by transfection with the total tumor DNA. Despite their persistence as episomes no infectious virus was produced. Furthermore, no viral antigens were detectable, although the SV40 messengers for the small and the large tumor antigens were present. These cells had, however, acquired the ability to form colonies in lower concentrations of serum. Thus this report provides, by restriction enzyme analysis, direct evidence for the presence of SV40 DNA in human tumors. (Author abstract) (34 Refs)

31. BK VIRUS-TRANSFORMED INBRED HAMSTER BRAIN CELLS. I. STATUS OF THE VIRAL DNA AND THE ASSOCIATION OF BK VIRUS EARLY ANTIGENS WITH PURIFIED PLASMA MEMBRANES.

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J Virol; 40(1):276-284 1981

Inbred LSH hamster brain cells were transformed in vitro by the GS strain of BK virus (BKV), and transplantable tumors classified as undifferentiated glioblastomas were induced in the syngeneic host. The viral status in the transformed cells, designated LSH-BR-BK, was established. About 46 genome equivalents per cell of viral DNA was detected, with the majority of sequences in a free form. The transformed cells expressed large quantities of tumor (T) antigen as well as surface (S) antigen as demonstrated by indirect immunofluorescence. Sixty-three percent of tumor-bearing hamsters produced high-titer antibodies against T, whereas 3 of 14 (21%) hamsters also produced antibodies against the BKV-specific S antigen. Furthermore, the relatedness of BKV early gene products, including T, S, and tumor-specific transplantation antigen, was established by the production of a rabbit antiserum against highly purified plasma membranes of LSH-BR-BK cells and by the induction of a BKV-specific tumor-specific transplantation antigen response by these plasma membranes in the syngeneic host. (Author abstract) (47 Refs)

32. INTEGRATION OF HEPATITIS B VIRUS DNA INTO THE GENOME OF LIVER CELLS IN CHRONIC LIVER DISEASE AND HEPATOCELLULAR CARCINOMA. STUDIES IN PERCUTANEOUS LIVER BIOPSIES AND POST-MORTEM TISSUE SPECIMENS.

Shafritz DA, Shouval D, Sherman HI, Hadziyannis SJ, Kew MC
Dept. Medicine, Liver Res. Center, Albert Einstein Coll. Medicine, 1300 Morris Park Ave., Bronx, NY, 10461
N Engl J Med; 305(18):1067-1073 1981

Recombinant-DNA technology combined with gel electrophoresis was used to find hepatitis B virus DNA (HBV-DNA) in liver and tumor tissue from patients with hepatocellular carcinoma and chronic liver disease, and to study integration of HBV-DNA into the genome of the tissue cells. HBV-DNA analysis was performed on hepatocellular carcinomas from 20 patients, all of whom had at least one serological marker indicating intercurrent or previous HBV infection. Twelve patients whose sera were positive for hepatitis B surface antigen (HBsAg) had integrated HBV-DNA in the tumor; 3/8 who were HBsAg negative but positive for antibody to HBsAg (anti-HBs) also had HBV-DNA integration. Five patients who were HBsAg negative but anti-HBs positive had no detectable HBV-DNA in their tumors. In some patients integrated HBV-DNA was also found in nontumorous liver tissue with the same or different hybridization pattern from that of tumor. In five HBsAg carriers with evidence of the carrier state and chronic liver disease for less than 2 yr, HBV-DNA was present but not integrated in liver tissue. In two patients who carried HBsAg for greater than 8 yr, HBV-DNA was integrated into the host genome. The studies suggest that integration of HBV-DNA into hepatocytes occurs during the course of persistent hepatitis B virus infection and precedes development of gross neoplasm. (22 Refs)

33. KAPOSI'S SARCOMA. IV. DETECTION OF CMV DNA, CMV RNA AND CMNA IN TUMOR BIOPSIES.

Boldogh I, Beth E, Huang ES, Kyalwazi SK, Giraldo G
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Int J Cancer; 28(4):469-474 1981

In order to determine whether human cytomegalovirus-(CMV) DNA homologous sequences as well as CMV-specific RNA(s) and antigen(s) exist in tumor biopsies of Kaposi's sarcoma (KS) DNA-DNA reassociation, RNA-DNA in situ cytohybridization and anticomplement immunofluorescence test (ACIF) tests were applied. Three of 10 DNAs extracted from Kaposi sarcoma biopsies contained DNA sequences homologous to radioactively labeled human CMV DNA probe. The amount of CMV DNA in these sarcoma tissues was calculated to range from 0.7 to 1 genome equivalent per diploid cell. The presence of virus-specific RNA was also demonstrated in sections from 5 of 10 tumor biopsies. CMV-determined nuclear antigen(s) (CMNA) present in variable degrees were also demonstrated. In contrast, we could not detect any herpes simple virus type II (HSV-2) or Epstein-Barr virus (EBV) DNA sequences in DNA of these tumor biopsies. Furthermore, there were no detectable HSV-2 or EBV-specific RNA or virus-specific antigens in sections of these biopsies. These results provide new lines of evidence for the relationship between CMV and Kaposi's sarcoma. (Author abstract) (34 Refs)

34. CHARACTERIZATION OF ANTIGENS IN SSV NONPRODUCER CELLS.

Thiel HJ, Matthews T, Broughton E, Butchko A, Bolognesi D
Dept. Surgery, Medical Center, Duke Univ., Durham, NC, 27710
Haematol Blood Transfus; 26:520-523 1981

In an attempt to identify putative transformation specific information coded by simian sarcoma virus (SSV), goat cells nonproductively transformed by SSV (SSV-NP) were isolated and inoculated several times as live cells into the same goat. The resulting hyperimmune serum (SSV-NP serum) was reacted in radioimmunoprecipitation against different transformed and nontransformed cell lines. After labeling SSV-NP cells with 3H-glucosamine and 35S-cysteine using a 7 hr pulse followed by a 14 hr chase, the respective tissue culture supernatants were immunoprecipitated with SSV-NP serum. The SSV-NP serum reacted specifically with two different molecules in SSV-NP cells, a SSV transformation-specific glycoprotein (SSV TrS-gp) and p65, which probably represents a modified gag-precursor. (7 Refs)

35. EVIDENCE THAT THE SPONTANEOUS BLASTOGENESIS OF LYMPHOCYTES FROM BOVINE LEUKEMIA VIRUS-INFECTED CATTLE IS VIRAL ANTIGEN SPECIFIC.

Thorn RM, Gupta P, Kenyon SJ, Ferrer JF
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Infect Immun; 34(1):84-89 1981

Cattle lymphocytes cultures for 3 days were found to spontaneously incorporate thymidine (3STI). Under optimal conditions of culture, the median magnitude of 3STI activity in lymphocytes from bovine leukemia virus (BLV)-infected cattle was higher than that of BLV-free cattle, but the ranges of the values overlapped. However, the 3STI activity of most BLV-infected cattle was specifically inhibited by serum containing BLV antibodies, whereas the 3STI activity of BLV-free cattle was not. The 3STI inhibitor copurified with Ig, and its activity could be absorbed with BLV. Rabbit anti-BLV serum inhibited 3STI, but rabbit anti-BLV p25 did not. These results indicate that BLV infection induces or expands a BLV-specific lymphocyte population. Spontaneous blastogenesis may be indicative of an immune response which controls virus spread. (Author abstract) (27 Refs)

36. PREVALENCE OF BOVINE LEUKEMIA VIRUS INFECTION IN FLORIDA.

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Dept. Preventive Medicine, Coll. Veterinary Medicine, Univ. Florida, Box J-136, Gainesville, FL, 32610
J Am Vet Med Assoc; 179(7):704-707 1981

A serologic study was undertaken to determine the prevalence of bovine leukemia virus (BLV) infection in dairy and beef cattle in Florida. Using the agar gel immunodiffusion test with a glycoprotein antigen, 47.8% of 7,768 dairy cattle and 6.7% of 4,911 beef cattle were found to have antibodies to BLV. The prevalence of BLV antibodies increased significantly (p greater than 0.0001) with increasing age. After data were adjusted for age, prevalence of BLV antibodies was significantly associated with dairy breed (p less than 0.05) but not with species (Bos taurus and B indicus) or sex. (Author abstract) (30 Refs)

37. FELINE LEUKEMIA VIRUS NONPRODUCER LYMPHOSARCOMAS OF CATS AS A MODEL FOR THE ETIOLOGY OF HUMAN LEUKEMIAS.

Hardy WD, McClelland AJ, Zuckerman EE, Snyder HW, MacEwen EG, Francis D, Essex M
No affiliation given
Haematol Blood Transfus; 26:492-494 1981

Immunological and epidemiological studies of feline lymphosarcoma (LSA) are summarized. Immunofluorescent antibody assay, immunodiffusion, tissue culture isolation, and radioimmunoassay were used to test 507 casts with LSA for feline leukemia virus (FeLV). FeLV-positive LSA was found in 360 cats; the remaining 147 had nonproducer (NP) LSA. No FeLV proteins or infectious viruses were detected in NP LSA. However, the FeLV-induced tumor specific oncovirus-associated cell membrane antigen was detected on the surface of both NP and FeLV positive LSA cells. Of 1,612 FeLV-exposed and -unexposed cats observed for development of LSA, 0/1,074 unexposed cats (observed av 3 yr/cat) developed LSA; 149/538 exposed cats (observed av 4.4 yr/cat) were persistently infected. LSA developed in 41 cats, 30 FeLV positive and 11 NP LSA. Difference in rate of NP LSA in FeLV-exposed and -unexposed cats was significant (p less than 0.001). FeLV appears to be the etiologic agent of feline LSA regardless of FeLV status. Mechanisms by which RNA- and DNA-containing viruses induce tumors are discussed. Feline NP LSA could be a useful model for elucidating mechanisms of oncovirus transformation. (12 Refs)

38. GENETIC APPROACHES TOWARD ELUCIDATING THE MECHANISMS OF TYPE-C VIRUS-INDUCED LEUKEMIA.

Aaronson SA, Barbacid M, Dunn CY, Reddy EP
Lab. RNA Tumor Viruses, NCI, Bethesda, MD, 20014
Haematol Blood Transfus; 26:455-459 1981

The mechanisms of induction of leukemia by murine type-C viruses was studied in newborn NIH/Swiss mice. Inoculations of 5 x 10(4) XC pock forming units of either Rauscher (R) or Moloney (M) murine leukemia virus (MuLV) produced gross enlargement of spleen and lymph nodes as early as 10-11 wk. RMuLV produced spleen enlargement and sometimes liver and peripheral or visceral lymph node enlargement. MMuLV produced thymus enlargement in most animals, and frequently affected other lymphoid organs. MMuLV-induced tumors were of T cell origin, as indicated by presence of Thy1 antigen and absence of Fc or C3 receptors. RMuLV-induced tumors were of B cell lineage, as indicated by presence of Fc receptors and absence of Thy1 antigen. Recombinant forms between oncogenic and nononcogenic type-C viruses were produced in wild mouse embryo cells of line WM-C. These recombinants contained genetic information in varying amounts from both parental viruses and exhibited varying degrees of oncogenicity. Results indicate that target cells for transformation by RMuLV and MMuLV contain specific markers distinguishing them from other lymphoid elements. The necessity of active virus replication for tumorigenesis by murine type-C viruses is suggested. (19 Refs)

39. IMMUNOPRECIPITATION OF INTRACISTERNAL A-PARTICLE-ASSOCIATED ANTIGENS FROM PREIMPLANTATION MOUSE EMBRYOS.

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JNCI; 67(5):1129-1134 1981

Murine intracisternal A-particles (IAP) are endogenous retrovirus particles expressed in large numbers in certain neoplastic tissues and during early stages of normal preimplantation mouse (outbred ICR) embryogenesis. IAP-associated antigens synthesized by preimplantation mouse embryos were precipitated by a rabbit (New Zealand White) antibody prepared against IAP from murine myeloma 104E. Characterization of the embryo immunoprecipitates with the use of one- and two-dimensional polyacrylamide gel electrophoresis revealed that a group of five proteins was synthesized by two- to eight-cell stages, but only three of these (mol wt of 67,000, 69,000, and 73,000) correlated with the morphologic expression of IAP in embryos. Only the proteins with mol wt of 75,000 and 77,000 were detected in morulae and blastocysts, when embryos were IAP-negative. This is the first biochemical identification of endogenous retrovirus-associated antigens in preimplantation mouse embryos. (Author abstract) (34 Refs)

40. IMMUNOLOGICAL CHARACTERIZATION OF A LOW ONCOGENIC MOUSE MAMMARY TUMOR VIRUS FROM BALB/CNIV MICE.

Vacquier JP, Cardiff RD, Blair PB
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J Virol; 40(1):56-64 1981

Antigenic determinants of mouse mammary tumor virus (MuMTV) from the low-mammary-tumor-incidence strain BALB/cNIV were compared by competition radioimmunoassay with those of MuMTV's isolated from several high- and low-mammary-tumor-incidence mouse strains, using rabbit hyperimmune sera against BALB/cNIV MuMTV and against MuMTV from the high-mammary-tumor-incidence strain BALB/cfC3H. Using anti-BALB/cfC3H serum in competition radioimmunoassay, BALB/cNIV MuMTV lacked antigenic determinants present on MuMTV's from the BALB/cfC3H, C3H, and GR strains. With anti-BALB/cNIV serum in competition radioimmunoassay, type-specific antigenicity was detected with BALB/cNIV MuMTV. We found class-specific antigenicities on BALB/cNIV MuMTV that were shared with RII and C3Hf MuMTV'S. BALB/cNIV MuMTV was reportedly derived from the C3Hf strain by infection of BALB/c mouse mammary tissue after transplantation into a (BALB/c x C3Hf)F1 hybrid followed by retransplantation into the BALB/c strain. However, BALB/cNIV MuMTV contained type-specific antigens not present on C3Hf MuMTV. The possible origin of these determinants is discussed. (Author abstract) (31 Refs)

TUMOR ASSOCIATED TRANSPLANTATION ANTIGENS

41. INDUCTION OF TUMOR RESISTANCE BY HYBRID CELL LINES BETWEEN HUMAN ACUTE LYMPHOCYTIC LEUKEMIA CELLS AND MOUSE MYELOMA CELLS.

Isobe K, Kawashima K, Watanabe E, Yamada K, Nagai Y, Nakashima I
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Gan; 72(5):705-712 1981

Three hybrid cell lines were derived from the fusion of BALB/c mouse NS-1 myeloma cells and human acute lymphocytic leukemia cells. Hybrid clones contained almost all of the mouse chromosomes and a few human chromosomes, and induced tumors in BALB/c and BALB/c nu/nu mice when inoculated sc. However, the tumors of BALB/c mice subsided spontaneously within 1 mo. The mice which survived the inoculation of 5 to approx 10 x 10(6) hybrid cells were able to reject a subsequent challenge with 5 x 10(6) NS-1 cells. Spleen cells or lymph node cells from immune mice were injected into BALB/c mice. These mice lived longer than the mice which received normal spleen cells or normal lymph node cells, when challenged with 5 x 10(6) NS-1 cells. These results suggest that a rearrangement of tumor-specific antigens on human/mouse hybrid cells can induce immunogenicity. (Author abstract) (20 Refs)

42. PREVENTION OF TUMORS IN RATS BY CROSS-PROTECTIVE IMMUNIZATION.

Fish DC, Bare AL, Djurickovic DB, Huebner RJ
NIH Intramural Res. Program, NCI Frederick Cancer Res. Center (FCRC), Frederick, MD, 21701
JNCI; 67(5):1041-1051 1981

F344 inbred rats were repeatedly immunized (days 0, 28, and 42) with normal syngeneic or allogeneic rat tissues or transplantable syngeneic or allogeneic rat tumors (some of which were virus producing). Immunized rats were challenged by sc injection of 10(5) or 10(6) syngeneic rat tumor cells from either of two different tumor lines. Successful cross-protective immunization prevented tumor development in rats that were challenged at 100-1,000x the 50% tumor dose. The protection was essentially lifelong and complete in that no tumors appeared up to 200 days post challenge in some experiments. To be successful, the tumor cell vaccines had to express a complement-fixing, cross-reacting antigen detected with sera from rats bearing any of several different tumors and to be able to induce a spontaneously regressing tumor in the host. (Author abstract) (34 Refs)

43. THE MECHANISM OF SPECIFIC SUPPRESSION IN EFFECTOR T CELL CLONES AGAINST TUMOR-ASSOCIATED TRANSPLANTATION ANTIGENS.

Fujiwara H, Tsuchida T, Mizuochi T, Kohmo T, Hamaoka T
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Gan; 72(5):732-741 1981

The present study investigates the fate of effector T cell population against tumor-associated transplantation antigens (TATA) of X5563 plasmacytoma in syngeneic mice rendered specifically unresponsive to the TATA. In this tumor system, T cell-mediated tumor-specific immunity was induced by id inoculation of viable tumor cells followed by the surgical resection of the tumor (immunization procedure). The iv presensitization of syngeneic hosts with X-irradiated tumor cells abolished the capability of those hosts to develop the tumor-specific immunity after the above appropriate immunization procedure. Spleen cells from the pretreated mice which subsequently received the immunization procedure could not regain the tumor-neutralizing activity after enzymatic treatment with papain. Moreover, lymphoid cells from the pretreated mice could not be stimulated by the immunization procedure even after proteolytic treatment with papain or trypsin, followed by transfer into other recipient mice free of the serum suppressive factor(s). On the other hand, such enzyme treatment was capable of preventing the tolerance induction of dinitrophenyl (DNP)-primed B cells after in vitro pulsing with DNP-D-GL (copolymer of D-glutamic acid and D-lysine) for 2 hr, suggesting that the enzymatic treatment used here was adequate to remove the blocked receptor and any tolerogen. These results suggest that in X5563 plasmacytoma system, the above specific unresponsiveness induced by the iv presensitization with TATA is due to the irreversible inhibition or deletion of effector T cell clones rather than mere effector cell blockade. (Author abstract) (24 Refs)

CLINICAL DIAGNOSTIC STUDIES

44. CELL SURFACE MARKERS AND KINETIC FEATURES IN ACUTE LYMPHOBLASTIC LEUKAEMIA.

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Cattedra de Patologia Medica I., C.so Polonia 14, 10126 Torino, Italy
Haematologica (Pavia); 66(4):419-425 1981

The labelling index (LI) of cell surface antigen SM+ and SM- blast cells from 15 patients (11 children: 7 males, 4 females; 2-11 yr old; 4 adults: 3 men, 1 woman; 23-37 yr old) with acute lymphoblastic leukemia (ALL) and from 1 patient with chronic myelocytic leukemia (CML) in lymphoid-like blast crisis was examined. In the four cases of SM+ ALL studied (3 T-cell ALL and 1 B-cell ALL), the LI of bone marrow blasts was 9.47 +-3.90 (range 6.1-16.7) compared with 1.38 +-1.19 (range 0.6-4.0, p less than 0.01) in the 11 cases of ALL without conventional T and B markers. Cells from the patient in a lymphoid-like blast crisis of CML had a bone marrow LI of 5.7. Upon combined immunofluorescent and autoradiographic analysis of bone marrow blasts, SM+ blast always displayed LI values significantly higher than SM- blasts. The data indicated that in acute leukemia blast cell populations, SM+ and SM- blasts have different LI. The relationship of this phenomenon to the problems of blast proliferation and differentiation are discussed. (16 Refs)

45. ANALYSIS OF THE CLINICAL AND BIOLOGICAL SIGNIFICANCE OF LYMPHOID PHENOTYPES IN ACUTE LEUKEMIA.

Greaves MF
Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England
Cancer Res; 41(11,part2):4752-4766 1981

Analysis of leukemia cell phenotypes using cell surface antigens and various enz ymes indicates that acute lymphoblastic leukemia (ALL) is a biologically heterogeneous disease consisting of four major subclasses with additional subsets existing within these subclasses. These different types of ALL appear to reflect sequential stages of early lymphocyte ontogeny.

There is a strong association between cell phenotype and first remission duration in ALL (p trend less than 0.0001) and an equally strong correlation between remission duration and WBC count at presentation. If common ALL and thymic ALL (T-ALL) are compared after adjustment of WBC counts, then the prognostic differences between these two major subclasses almost disappear (p = 0.38). It is suggested, therefore, that an immunological (and enzymatic) phenotype of ALL subclasses may not be an independent correlate of prognosis but nevertheless is linked to other differentiation-linked features, especially growth rate and sites of clonal expansion (eg, marrow versus thymus), which critically influence the size of the clonogenic leukemic population and its associated evolutionary status with respect to drug-resistant mutants at the time of diagnosis and introduction of therapy. An extensive library of monoclonal antibodies has been used to further define the phenotypic heterogeneity of T- and non-T ALL. Several of the antigenic structures identified by these monoclonal antibodies have been isolated and characterized. T-ALL can be dissected into several subsets - corresponding to stages of intrathymic differentiation. Non-T ALL (null-ALL, common ALL, and B-ALL) all have a phenotype indicative of B-lineage affiliation indicating that 'non-T, non-B' ALL may originate from B-cell precursors in bone marrow. A cell type is identified in normal bone marrow which has the same identical monoclonal antibody-defined phenotype as common ALL and may provide the target cell for this disease. (Author abstract) (94 Refs)

46. DEFINITION OF THE HIGH-RISK ACUTE LYMPHOBLASTIC LEUKEMIA PATIENT BY IMMUNOLOGICAL PHENOTYPING WITH MONOCLONAL ANTIBODIES.

Zipf TF, Fox RI, Dilley J, Levy R
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Cancer Res; 41(11,part2):4786-4789 1981

An accurate method of classification of the surface membrane characteristics of blast cells from patients with acute lymphoblastic leukemia would allow a more definitive study of the nature of this disease. Monoclonal antibodies have been produced to the surface antigens of leukemic blasts from a patient with high-risk acute lymphoblastic leukemia. Two antibodies of interest were obtained from this immunization. These two, in combination with a monoclonal antibody with anti-Ia specificity, have been used to obtain surface phenotypes for patients with childhood acute lymphoblastic leukemia. Preliminary results indicate that the definition of a high-risk group, using these antibodies, is possible. (Author abstract) (16 Refs)

47. IMMUNOLOGICAL DEFINITION OF LEUKEMIC CELL SURFACE PHENOTYPES.

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Cancer Res; 41(11,part2):4790-4793 1981

Immunological phenotyping of blasts from over 200 children with acute lymphocytic leukemia (ALL) reveals both interpatient differences and phenotypic heterogeneity in the blast population from individual patients. A battery of five independent lymphocyte differentiation markers, RBC-forming rosettes, T-cell antigens, Ia-like antigens, the common ALL antigen, and surface Ig, permit classification of all ALL specimens into four major marker groups. These are common, T-cell, B-cell, and undifferentiated ALL. Heterogeneity in the marker phenotypes within each of the major groups is observed. Within individual RBC receptor-positive ALL specimens, phenotypic heterogeneity in the blast population is demonstrated. Sequential determinations of the blast phenotype during periods of active disease reveal a second example of intrapatient blast cell heterogeneity. Differences in phenotype of the dominant blast populations present prior to treatment and at relapse are observed in sequential studies of individual patients. These shifts in phenotype are nonrandom. They result most frequently from losses in single differentiation markers. A unifying hypothesis which explains these observations of phenotypic heterogeneity is that ALL blasts manifest limited lymphoid-like differentiation. (Author abstract) (8 Refs)

48. SOUTHWEST ONCOLOGY GROUP EXPERIENCE WITH IMMUNOLOGICAL PHENOTYPING IN ACUTE LYMPHOCYTIC LEUKEMIA OF CHILDHOOD.

Pullen DJ, Falletta JM, Crist WM, Vogler LB, Dowell B, Humphrey GB, Blackstock R, Van Eys J, Cooper MD, Metzgar RS, Meydrech EF
Operations Office, Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas city, KS, 66103
Cancer Res; 41(11,part2):4802-4809 1981

The Pediatric Division of the Southwest Oncology Group is attempting to define subgroups of acute lymphoblastic leukemia (ALL) by laboratory delineation of marrow lymphoblast characteristics at diagnosis. Immunological subclassification studies include erythrocyte-forming rosette (E-rosette), C^3 receptor, Fc receptor, surface Ig (Sig) and cytoplasmic Ig (CIg) determinations, as well as peripheral T (PT), thymocyte, Ia, and common ALL membrane antigen testing. Four subgroups of ALL have thus far been defined: null (SIg-, CIg,-, PT-); pre-B (SIg-, CIg+, PT-); B-cell (SIg+, CIg-, PT-); and T-cell (SIg-, CIg-, PT+). A group of 118 patients have had complete testing, and an additional 121 patients have had partial testing. Thirty-five patients with pre-B ALL and 27 patients with T-cell ALL have thus far been studied. Pre-B and null types of ALL appear closely related in multiple subclassification parameters (age, sex, p hysical findings, WBC count, and lymphoblast Ia and common ALL antigen positivity). Pre-B ALL patients treated with the same treatment regimens as were null ALL patients appear to have shorter durations of complete remission, although the difference has not yet reached statistical significance. Results suggest that the male predominance and older age distribution previously recognized for E-rosette-positive T-cell leukemia can also be expected in the E-rosette-intermediate and E-rosette-negative T-cell ALL subsets, although statistically higher WBC counts at diagnosis are seen in the E-rosette-positive subset. Mediastinal mass at diagnosis is most likely in the patient with E-rosette-positive, thymocyte antigen-positive lymphoblasts. The E-rosette intermediate and E-rosette negative, as well as the E-rosette positive, T-cell ALL subsets appear to constitute poor prognosis categories. Correlation with treatment results is preliminary in all groups but suggests that stratification of ALL at diagnosis according to several immunological subgroupings may prove helpful in planning therapy. (Author abstract) (32 Refs)

49. EXPRESSION OF THE OKT MONOCLONAL ANTIBODY DEFINED ANTIGENIC DETERMINANTS IN MALIGNANCY.

Greaves M, Delia D, Sutherland R, Rao J, Verbi W, Kemshead J, Hariri G, Goldstein G, Kung P
Membrane Immunology Lab., Imperial Cancer Res. Fund, London WC2A 3PX, England
Int J Immunopharmacol; 3(3):283-299 1981

Cellular specificity in human leukemia of murine monoclonal antibodies OKT1, 3, 4, 6, 8, 9, 10, 11, and 11A were screened by microscopic and flow cytometric immunofluorescence methods and 125I-binding assays. Tests against malignant T cells showed a correlation between phenotype and clinical diagnosis. T cells from acute lymphoblastic leukemia (T-ALL) cells always showed an immature phenotype. Non-Hodgkin T lymphoma cells showed a cortical thymic phenotype. Both cell types appear to originate from T cell precursors. Cells from chronic T leukemias and cutaneous T lymphomas and leukemias that occur primarily in older adults showed mature T cell phenotypes. OKT11 and OKT11A reacted similarly with sheep E rosettes and appear to react to the same structures. Several T-ALL cell lines were modified in vitro to a more mature phenotype by 12-O-tetradecanoylphorbol 13 acetate or other inducers. This was demonstrated by binding of OKT1, 8, 9, 11, and other antibodies. OKT9 reacted preferentially with T leukemias, but was not T-specific, binding also to other leukemia cells and to other malignant tumor types. Cells induced to mature in vitro lost the OKT9 determinant. OTK9 bound to a receptor that may be a marker for malignancy. OKT10 bound to leukemias and normal bone marrow cells of the myeloid and B cell lineages. OTK6 bound to neuroblastoma cells. (43 Refs)

50. A HYPOTHESIS ON THE ETIOLOGY OF ADULT T-CELL LEUKEMIA/LYMPHOMA.

Tajima K, Tominaga S, Shimizu H, Suchi T
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Gan; 72(5):684-691 1981

The results of the nationwide survey performed by the T- and B-cell Malignancy Study Group revealed that adult T-cell leukemia/lymphoma (ATLL) was prevalent in limited zones in Kyushu, mainly in coastal areas, warm in winter and humid in summer. It was found that the geographical distribution of filariasis was very similar to that of ATLL. It is known that filariasis affects lymphatic vessels and results in several lymphoreticular ailments, and microfilaria is transmitted by mosquitoes infected with some kinds of not yet fully identified viruses. From analyses of the time trends of the av wt and height of school children by prefecture, it is suggested that the nutritional condition of inhabitants in Kyushu might have been poorer than that of inhabitants of other areas in Japan, especially in the past. In order to elucidate the etiology of ATLL, relevant geographic-pathological information and other related information was accumulated and an etiological hypothesis was formulated. It was hypothesized that repeated exposure to filarial antigen and some viruses might have played an important role in the etiology of ATLL and that undernutrition had also contributed to the progression of ATLL. (Author abstract) (31 Refs)

51. DERIVATION OF HUMAN T-CELL LEUKEMIAS.

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Cancer Res; 41(11,part2):4767-4770 1981

Cell surface antigenic changes occur during the stages of T-cell ontogeny in several animal model systems. In the present study, multiple monoclonal antibodies were developed to human thymocyte and T-cell surface differentiation antigens as a means of probing T-cell ontogeny in humans. It was shown that three distinct stages of human intrathymic differentiation exist and that the mature inducer (T4 +) and suppressor (T5 + / TH2 +) T-cell subsets arise at specific points during these maturation events. Moreover, T-cell leukemias can now be related to the three stages of the thymic compartment or, alternatively, the more differentiated peripheral T-cell compartment. (Author abstract) (28 Refs)

52. MARKER PROFILES OF LEUKEMIA-LYMPHOMA CELL LINES.

Minowada J
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Haematol Blood Transfus; 26:323-325 1981

Marker profiles (eg, Ia antigen, myelomonocyte antigen, immunoglobulins, Epstein-Barr virus) of 50 leukemia-lymphoma cell lines are presented. The cell lines are divided into three groups: T cell, B cell, or non-T, non-B cells. (4 Refs)

53. REGULATION OF HUMAN T-CELL PROLIFERATION: T-CELL GROWTH FACTOR AND ISOLATION OF A NEW CLASS OF TYPE-C RETROVIRUSES FROM HUMAN T-CELLS.

Gallo RC, Poiesz BJ, Ruscetti FW
NCI, Bethesda, MD, 20014
Haematol Blood Transfus; 26:502-514 1981

Recent results with human T-cell growth factor (TCGF), the various T cell systems, and the isolation of a new type-C retrovirus released from growing T-cells from some of these T-cell neoplasias are summarized. Unlike normal T-cells, neoplastic mature T-cells respond directly to TCGF without prior lectin or antigen in vitro activation. Transformed T-cell lines exhibit phenotypic characteristics consistent with the neoplastic cells of their disease of origin. A new retrovirus, human T-cell lymphoma-leukemia virus (HTLV) was isolated from fresh and cultured cells from two patients, each with a variant of a cutaneous T-cell lymphoma. Further studies showed that HTLV was not significantly related to any known animal retrovirus, is not an endogenous (genetically transmitted) virus of man, and at present is only associated with fresh or cultured T-cells from patients with the T-cell neoplasia. The results suggest that HTLV infected some mature T-cells of some people and may be involved in some neoplasias involving these cells. (33 Refs)

54. SEROLOGIC SUBTYPING OF CALL.

Becker WM, Schmiegel WH, Kabisch H, Arndt R, Thiele HG
(c/o Kabisch) Abt. fur Hamatologie und Onkologie, Universitats-Kinderklinik, Martinistrasse 52, 2000 Hamburg 20, W. Germany
Haematol Blood Transfus; 26:329-331 1981

Rabbit antisera against common acute lymphoblastic leukemia antigen (Ag cALL) were produced by repeated injections of lectin-purified antigens. The antisera were found to discriminate among subsets of cultured cALL cells that released Ag cALL into the culture medium. (6 Refs)

55. CARDIAC MYXOMA (ENDOCARDIOMA). AN IMMUNOCYTOCHEMICAL ASSESSMENT OF HISTOGENESIS.

Morales AR, Fine G, Castro A, Nadji M
Dept. Pathology, Univ. Miami Sch. Medicine, P.O. Box 016960, Miami, FL, 33101
Hum Pathol; 12(10):896-899 1981

Eighteen cardiac myxomas having a variety of histologic patterns were stained for factor VIII related antigen utilizing the peroxidase-antiperoxidase technique. Regardless of their histologic appearance, intense reactivity for factor VIII related antigen was found in tumor cells, whereas four other intracardiac tumors did not stain. Since factor VIII related antigen is known to be elaborated only by endothelial cells and megakaryocytes, it is concluded that cardiac myxoma cells, which similarly synthesize this antigen, originate from endothelial or endocardial cells. (Author abstract) (12 Refs)

56. IMMUNOLOGIC DETECTION OF EAR-NOSE-THROAT TUMORS.

Kessler L, Knothe J, Irmscher H
HNO-Klinik, Medizinische Akademie 'Carl Gustav Carus', Fetscherstrasse 74, DDR-8019 Dresden, E. Germany
Laryngol Rhinol Otol (Stuttg); 60(8):402-404 1981

The diagnostic efficacy of the macrophage electrophoretic mobility (MEM) test with human encephalitogenic protein (HEP) as antigen was studied in 31 patients with ear-nose-throat tumors, 108 patients with tumors of other localizations, and 116 tumor-free controls. Laryngeal carcinoma was diagnosed in 21/31 patients, hypopharyngeal carcinoma in 2, tonsillar carcinoma in 2, carcinoma of the tongue in 2, and other tumors in 4. Colorectal carcinoma was diagnosed in 27/108 patients with other tumors, gastric carcinoma in 32, hypernephroid carcinoma in 6, breast carcinoma in 18, and other tumors in 25. The MEM test was false positive in 17.7% of the tumor-free controls, ie, the selectivity was 82.3%. The MEM test was positive in 77.8-100% of the 139 tumor patients, av 83.7%. The av percentage of positive MEM tests was 89.3% for the 31 patients with ear-nose-throat tumors. (10 Refs) (In GER)

57. SEROLOGICAL DETECTION OF TUMOR ANTIBODIES IN THE SERA OF PATIENTS WITH LARYNGEAL CARCINOMA.

Blume N, Milatovic D
Klinik und Poliklinik fur Hals-, Nasen- u. Ohrenkranke rechts der Isar, TU Munchen, Ismaninger Str. 22, 8000 Munich 80, W. Germany
Laryngol Rhinol Otol (Stuttg); 60(8):405-406 1981

Sera of 20 patients with squamous-cell carcinoma of the larynx were evaluated for the presence of antibodies against a soluble antigen from cultured laryngeal carcinoma cells by the enzyme-linked immunosorbent assay. Stage T1N0M0 was diagnosed in 5 cases, T2N0M0-T4N0M0 in 3, and T2N1M0-T4N2M0 or recurrence in 12. Sera from 121 healthy subjects served as controls. The antibody levels of the sera from the tumor patients were significantly higher than those in the controls, and the antibody levels increased with advancing tumor stage. Immune response was also observed in 55% of the control sera. (7 Refs) (In GER)

58. HUMAN MAMMARY EPITHELIAL ANTIGENS (HME-AGS) IN THE CIRCULATION OF NUDE MICE IMPLANTED WITH A BREAST TUMOR AND NON-BREAST TUMORS.

Sasaki M, Peterson JA, Wara WM, Ceriani RL
(c/o Ceriani) Bruce Lyon Memorial Res. Lab., Children's Hosp. Medical Center, 51st and Grove St., Oakland, CA, 94609
Cancer; 48(10):2204-2210 1981

Human mammary epithelial antigens (HME-Ags) obtained from the membrane of the human milk fat globule (HMFG) were tested for their possible role as breast tumor markers. Specific antisera raised against HME-Ags were used to monitor plasma concentrations of these antigens in nude mice implanted with a human breast tumor. The level of plasma HME-Ags, determined by radioimmunoassay, was significantly higher in animals transplanted with a human breast tumor (mean +- standard error; 687 +-184 ng/ml) than those with other types of human tumors (colon carcinoma: 50 +-29; lung carcinoma: 82 +-78; medulloblastoma: less than 30; and Wilson melanoma: less than 30) and healthy control animals (49 +-22). Removal of the breast tumor resulted in a significant drop of HME-Ags level to 'background' values, suggesting that animals with the breast tumor did release into the circulation HME-Ags which could be possibly used as breast-tumor markers in breast tumor diagnosis. (Author abstract) (24 Refs)

59. USE OF AN ELECTROIMMUNODIFFUSION METHOD ON CELLULOSE ACETATE FILMS FOR THE DETECTION OF ANTIGENICITY IN HUMAN BREAST CANCER THAT IS RELATED TO THE MAJOR CORE ANTIGEN OF MOUSE MAMMARY TUMOR VIRUS (MUMTV).

Kryukova IN, Komarova E, Zotter S, Grossmann H
All Union Cancer Res. Center, Acad. Medical Sciences, Kashirskoye Chausse 6, Moscow 115478, USSR
Arch Geschwulstforsch; 51(6):517-521 1981

The method developed by Abelev was used for detection of MuMTV-related antigens in tumor tissue and sera of breast cancer patients. The highly sensitive electroimmunodiffusion method on acetate films employed isotachophoresis. In 2/5 breast cancer extracts, protein fractions of about 50,000 mol wt exhibited antigenicity related to the major core antigen of MuMTV (p27). This antigenicity was not detected in the patients' sera. (18 Refs)

60. THE ABO(H) CELL SURFACE ANTIGENS IN CARCINOMA AND BENIGN LESIONS OF THE BREAST.

Shull JH, Javadpour N, Soares T, DeMoss EV
(c/o Javadpour) Surgery Branch, NCI, Bethesda, MD, 20205
J Surg Oncol; 18(2):193-196 1981

The ABO(H) cell surface antigens of 13 breast carcinomas and 17 benign breast lesions were tested with a specific red cell adherence assay (SRCA). All 13 breast carcinomas, including 2 lobular carcinomas in situ and 1 noninfiltrating ductal carcinoma, had lost their ABO(H) surface antigens. Fourteen of 17 benign lesions had retained their ABO(H) surface antigens. The benign lesions losing their antigens were one case each of atypical intraductal hyperplasia, sclerosing adenosis, and intraductal papilloma. SRCA may be a predictor of which benign breast lesions are in fact premalignant. (Author abstract) (9 Refs)

61. SYNTHESIS OF ABH BLOOD GROUP SUBSTANCES IN BLADDER TUMOURS.

Fujita J, Matsumoto K, Kishi K, Ishiyama I
Dept. Urology, Kyoto Univ., Konoe-cho, Yoshida, Sakyo-ku, Kyoto 606, Japan
Br J Urol; 53(5):448-452 1981

A specific red cell adherence test which can detect the cell surface ABH blood group antigens was performed on formalin-fixed frozen sections of 38 bladder tumors. In 27 tumors decreased glycosyltransferase activity was suggested, but the site and the degree of the blockade did not seem to be identical in every tumor. Blood group A and B tumors could be grouped into four types according to the presence of these three isoantigens. One group which showed A or B but no H activity (Type I) consisted only of Grade 1, superficial tumors. All of the invasive tumors belonged to other types. For blood group O tumors no clear-cut correlation could be found between malignancy of the tumor and the presence of H activity. Eight of 22 Grade 2 or 3 tumors and 9 of 21 invasive tumors retained the isoantigen, which seemed to invalidate the use of this test as a predictive indicator. Only where blood group A or B patients were concerned, and the presence of H activity was regarded as abnormal as well as the absence of A and B, could all grade 2 or 3 tumors and all invasive tumors be detected by this test. (Author abstract) (14 Refs)

62. THE VALUE OF THE ERYTHROCYTE ADHERENCE TEST (SRCA TEST) FOR DIAGNOSIS AND THERAPY FOR SUPERFICIAL TRANSITIONAL CELL CARCINOMA OF THE BLADDER.

Jakse G, Hofstadter F
Universitatsklinik fur Urologie, Anichstrasse 35, A-6020 Innsbruck, Austria
Helv Chir Acta; 48(3/4):499-501 1981

The erythrocyte adherence test (SRCA test) for detection of ABO blood group antigens was used to study 356 patients with superficial transitional cell carcinomas of the urinary bladder. ABO-positive patients (ABO+) had dysplasia in only 23% of cases. ABO-negative patients (ABO-) had dysplasia or carcinoma in situ in approx 50% of cases. Retrospective examination of biopsy material showed 83% of histologically normal bladder mucosa as ABO+, but only 10% of dysplasia or carcinoma samples as ABO+. In a prospective study 69 patients were given chemoprophylaxis with adriamycin after transurethral resection of superficial transitional cell tumors. Biopsy material from 29 patients showed 11 as ABO+ and 18 as ABO-. The recurrence rate in both groups was the same. However, the recurrence of progressive tumors in the ABO- group (16%) was significantly reduced by adriamycin treatment from the published rate for ABO- patients (70%). (6 Refs) (In GER)

63. THE CURRENT STATUS OF RADIOIMMUNOASSAY (RIA) OF PROSTATIC ACID PHOSPHATASE IN THE EVALUATION OF CARCINOMA OF THE PROSTATE.

Huber PR, Hagmeier V, Scholer A, Lyrer P, Christen P, Wolf T, Kanszo G, Hassel JP, Rutishauser G
Hormonlabor Frauenklinik, Kantonsspital, Schanzenstrasse 46, CH-4031 Basel, Switzerland
Helv Chir Acta; 48(3/4):445-452 1981

Results of radioimmunoassay (RIA) of prostatic acid phosphatase (PAP) were compared with results from enzymatic assay (EA) using thymolphthalein monophosphate as substrate. EA measured enzymatic activity of PAP in terms of IU/liter, while RIA measured amount of protein, including inactive forms retaining their antigenic specificity, in terms of wt. RIA produced approx 50% better recognition of malignant growth (approx 55%) than EA (23%) in patients with untreated carcinoma. False positives were higher with RIA (approx 20%) than with EA (approx 10%), lowering overall success with RIA to approx 30%. In patients with treated carcinoma pathological levels of PAP were found in approx 45% with RIA and 20% with EA. Positive results were obtained in assay of bone marrow samples from one healthy patient and from a patient with myeloid leukemia. Differences between results from serum and bone marrow samples were attributed to effects if dilution. RIA apparently produced better overall results than EA, but at higher financial cost. (1 Ref) (In GER)

64. ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY FOR CULTURED AUTOLOGOUS MELANOMA CELLS.

Livingston PO, Michitsch R, Shiku H, Pinsky CM, Oettgen HF
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cell Immunol; 64(1):131-143 1981

Sera from 33 patients with malignant melanoma were tested for antibody-dependent cell-mediated cytotoxicity (ADCC) against cultured autologous melanoma cells prelabeled with [3H]proline in a 36-hr assay. Effector cells (autologous or from normal donors) were obtained by Ficoll-Hypaque separation of peripheral blood. Assay sensitivity (but not specificity) was affected by the effector cells used, the optimal source of effector cells varying between different autologous serum-target cell combinations. The activity of autologous effector cells appeared to correlate inversely with the extent of disease. Sera from 18 patients gave positive direct tests. In seven cases reactivity was strong enough to permit analysis of specificity with absorption tests. Serum from one patient recognized a melanoma antigen restricted to autologous melanoma cells and three other melanoma cell lines, and not present on other melanoma cell lines or autologous tissues, nonmelanoma tumor cells, or xenogeneic cells. Sera from five patients detected a diverse group of widely distributed antigens, all related to fetal calf serum (FCS). Serum from the seventh patient reacted with a widely distributed antigen not related to FCS. (Author abstract) (21 Refs)

65. EVALUATION OF THE LEUCOCYTE ADHERENCE INHIBITION ASSAY IN THE DIAGNOSIS OF COLORECTAL CARCINOMA.

Leveson SH, Woodhouse LF, Giles GR
Univ. Dept. Surgery, St. James's Univ. Hosp., Leeds LS9 7TF, England
Clin Oncol; 7(3):183-191 1981

A prospective trial has been established in order to assess the accuracy of the leukocyte adherence inhibition (LAI) assay in diagnosing colorectal carcinoma. Estimates were performed on 26 patients with colorectal cancer, 22 patients with cancer of non-colorectal origin and 22 patients with benign disease. The results suggest that the assay is very accurate and specific in early cancer, but that the results become less reliable with increasing tumor burden. Practical problems associated with antigen preparation and storage are discussed. (Author abstract) (16 Refs)

OTHER RELATED STUDIES

66. THE NETWORK CONCEPT AND LEUKEMIA.

Eichmann K
Krebsforschungszentrum - Immunologie, Im Neuenheimer Feld 280, 6900 Heidelberg, W. Germany
Haematol Blood Transfus; 26:343-344 1981

Application of the network concept to leukemia is discussed. Network regulation may represent a major mechanism for maintenance of steady state in the immune system. The immune system can be viewed as a series of idiotypic and anti-idiotypic compartments that regulate one another, regulation is determined by effector functions of antigen-specific elements in each compartment. Relevance to leukemia is noted: (1) unbalances in network control make certain lymphocytes susceptible to neoplastic transformation (eg the Balb/c mouse myelomas with antiphosphorylcholine specificity and T15 idiotype), and (2) specific immune therapy could involve recovery of normal T cells from leukemia patients and restimulation in vitro with leukemic cells from the same patient (restimulation methods would seek a high proportion of cytotoxic T cells with specificity for idiotypic determinants on the leukemic cells). The network concept reveals nonspecific manipulation of the immune system to be worthless; only antigen-specific measures could be expected to disturb the balance toward generation of desired effector functions. (3 Refs)

67. COMPARISON OF THE HEMOCYTOMETER AND TUBE MODIFICATIONS OF THE LEUKOCYTE ADHERENCE INHIBITION ASSAY - II. APPLICATION OF BOTH MODIFICATIONS FOR DETECTION OF ANTITUMOR IMMUNITY IN MAN.

Schimke R, Holan V, Sibl O, Hasek M, Ambrosius H
Section Biosciences, Lab. Immunobiology, Karl-Marx-Univ., 7010 Leipzig, E. Germany
Neoplasma; 28(3):257-264 1981

The hemocytometer and the tube modifications of the WBC adherence inhibition (LAI) assay were compared under identical experimental conditions in patients with carcinoma of the larynx. In the direct test, both modifications showed adherence inhibition if patients peripheral blood WBC (PBL) were incubated with a larynx cancer antigen preparation. Cell-free supernatants obtained by cocultivation of patients PBL with the antigenic extract yielded positive results only in the hemocytometer modification. Those supernatants inhibited the adherence of both normal human PBL and guinea pig peritoneal cells. Human encephalitogenic protein used as antigenic preparation in both direct and indirect hemocytometer modifications caused changes in adherence too. The presented results confirm the opinion that the hemocytometer and tube LAI assays base on different mechanisms. (Author abstract) (24 Refs)

68. CLONAL PROLIFERATION OF CULTURED NONMALIGNANT AND MALIGNANT HUMAN BREAST EPITHELIA.

Smith HS, Lan S, Ceriani R, Hackett AJ, Stampfer MR
Dept. Surgery, Albert Einstein Coll. Medicine, Bronx, NY, 10461
Cancer Res; 41(11,part1):4637-4643 1981

We have developed a method for clonal growth of human mammary epithelial cells of both nonmalignant and malignant origin. Plating efficiencies of 1 to 50% were obtained by seeding second-passage mammary epithelial cells on fibroblast feeder layers in an enriched medium composed of various hormones and growth factors, as well as conditioned media from three specific human cell lines. Single mammary epithelial cells seeded sparsely onto the fibroblasts underwent at least eight population doublings to form large, readily visible colonies. Optimal colony formation required both feeder cells and the enriched medium. Epithelial colonies containing at least 16 cells were visible 5 days postseeding, and these colonies continued to grow progressively. Plating efficiency and colony size were similar on UV-irradiated or nonirradiated fibroblasts. The number of colonies formed was proportional to the number of epithelial cells plated. The colonies were identified as epithelial by the presence of human mammary epithelial antigens. (Author abstract) (31 Refs)

69. HUMAN SQUAMOUS CELL CARCINOMA. ESTABLISHMENT AND CHARACTERIZATION OF NEW PERMANENT CELL LINES.

Krause CJ, Carey TE, Ott RW, Hurbis C, McClatchey KD, Regezi JA
Dept. Otorhinolaryngology, Univ. Michigan Hosp., Ann Arbor, MI, 48109
Arch Otolaryngol; 107(11):703-710 1981

Squamous cell carcinoma is the most common of human cancers, and yet because it is poorly represented by cultured cell lines, little is known about the characteristic cell biology and the cell-surface antigenic phenotypes of such tumors. To develop a continuously available source of squamous cell carcinoma for repeated and reproducible serologic analysis and for better understanding of its biologic characteristics, tissue culture methods and nude mice were used to establish new cell lines of squamous carcinoma. Special media, serum supplements from several sources, and methods of handling fresh tissue specimens were all examined as a means of improving the survival of tumor cell lines. Several new cell lines were established. Features characteristic of a squamous cell origin, eg, microvilli, desmosomes, tonofilaments, and the squamous cell differentiation antigen (pemphigus antigen), were found. The clinical course of disease in individual donor patients has been examined. (Author abstract) (7 Refs)

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DETECTION/ CHARACTERIZATION/ ISOLATION

1. COMPARISON OF HISTOLOGIC AND IMMUNOLOGIC HETEROGENEITY OF NON-HODGKIN'S LYMPHOMAS.

Borowitz MJ, Croker BP, Metzgar RS
Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710
Am J Pathol; 105(2):97-106 1981

The lymphocyte surface marker phenotype in 11 selected cases of non-Hodgkin's lymphomas was determined with anti-Ig and mouse monoclonal antibodies against human lymphocyte antigens. A complement-mediated cell cytotoxicity assay on suspensions of the tumor cells was compared with an indirect immunoperoxidase technique on frozen tissue sections. Both methods gave good results in tumors with a uniform cell population, but the frozen section technique was superior in heterogeneous tumors. The six B-cell neoplasms were heterogeneous with respect to expression of surface Ig and Ia antigens. The five T-cell tumors were morphologically heterogeneous and also highly variable in their expression of different T-cell specific antigens. (Author abstract) (33 Refs)

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2. CHARACTERISTICS AND DISTRIBUTION OF A 25,000 DALTON ANTIGEN DEFINED BY A MONOCLONAL ELICITED TO COMMON ACUTE LYMPHOBLASTIC LEUKEMIA CELLS (MEETING ABSTRACT).

Jones NH, Metzgar RS
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

A Balb/c mouse was immunized serially over a six wk period with cells from five patients with common acute lymphoblastic leukemia (cALL) cells. Three days after the last injection the spleen cells from this mouse were fused with the IgG1-secreting mouse myeloma cell line P3-X63-Ag8. After two wk hybridoma colonies were visible and the culture supernatants were screened for antibody binding by a complement-dependent microcytotoxicity assay. One hybridoma, DU-ALL-1, reacted with the cALL cell lines REH and NALM-1, but did not react with any of the T or B lymphoblastoid cell lines tested or with U937, a monocytic leukemia cell line, K562, an erythroleukemia cell line, or HL-60, a myeloid leukemia cell line. Cytotoxicity and indirect immunofluorescent testing of human leukemia cells showed that DU-ALL-1 reacted with cells from a majority of cALL patients (65/71) and with cells from some patients with acute myeloblastic leukemia (5/8). Cells from some non T, non B ALL donors reacted with DU-ALL-1 and not with J-5 antiserum (a monoclonal antibody to the 98,000 daltons cALL antigen), while cells from other donors gave reciprocal reactivity. DU-ALL-1 antibody was generally non-reactive with cells from patients with chronic lymphocytic leukemia (0/8), chronic myelogenous leukemia in blast crisis (0/2), and T-ALL (1/14). Analysis by sodium dodecyl sulfate-polyacrylamide gel electrophoresis showed that an antigen with an apparent mol wt of 25,000 daltons was immunoprecipitated from surface radioiodinated and detergent-solubilized NALM-1 cells by DU-ALL-1 antibody. A similar 25,000 mol wt antigen was also precipitated by DU-ALL-1 from radioiodinated membrane antigens from normal platelets, and DU-ALL-1 positive lymphoid and myeloid leukemia cells. The results indicate that DU-ALL-1 monoclonal antibody is able to subclassify human lymphoid and myeloid leukemias and the antigen probably represents a previously undefined 'differentiation-type' antigen. (no Refs)

3. MONOCLONAL ANTIBODY-DEFINED HUMAN LUNG CELL SURFACE PROTEIN ANTIGENS.

Mazauric T, Mitchell KF, Letchworth GJ, Koprowski H, Steplewski Z (c/o Steplewski), Wistar Inst. Anatomy and Biology, Philadelphia, PA, 19104
Cancer Res; 42(1):150-154 1982

Monoclonal antibodies were used to define four distinct antigens present on the surfaces of human lung tumors. Immunoprecipitation of the four antigens by monoclonal antibodies and sodium dodecyl sulfate:polyacrylamide gel electrophoresis reveals that they have distinct complex structures. Different patterns of expression of these antigens on cells of other than lung tumor origin were detected by the same panel of monoclonal antibodies. (Author abstract) (11 Refs)

4. STUDIES ON A PURIFIED HUMAN LUNG TUMOR-ASSOCIATED ANTIGEN (MEETING ABSTRACT).

Braatz JA, Scharfe TR, Princler GL, McIntire KR
National Cancer Institute, Bethesda, MD, 20205
Oncodev Biol Med; AbstractsBook,1:54 1981

LT-109, is immunochemically related to serum alpha 1-antichymotrypsin (ACT), although it lacks chymotrypsin-inhibitory activity and differs in size and charge from ACT. Another, which is not related to ACT or LT-109, can be demonstrated by double diffusion techniques to be present in 84/98 lung tumor extracts, but not in normal tissues. This antigen, designated LT-120, can be quantitated by a radial immunodiffusion assay and has been purified from a crude lung tumor extract to apparent homogeneity. LT-120 exhibits size and charge heterogeneity but all forms are antigenically identical. The predominant form in the tumor extract was 150,000 daltons by gel filtration and 81,000 daltons by sodium dodecyl sulfate gel electrophoresis. The purified antigen could be radioiodinated with Bolton-Hunter reagent but not with chloramine-T or lactoperoxidase-catalyzed labeling or diazotized iodosulfanilic acid. A similar antigen has been identified and purified from CHAGO, a human lung cancer cell line. Antigenically identical to LT-120, the CHAGO antigen also exhibits size/charge heterogeneity and resistance to chloramine-T mediated iodination; however, by gel filtration it has a size of 50,000. Preliminary results suggest the antigen is present in serum and urine from lung cancer patients at higher levels than in normal individuals. The various forms are being elevated for their biochemical and immunochemical properties and for their usefulness as a lung tumor marker. (no Refs)

5. BIOCHEMICAL CHARACTERIZATION AND CLINICAL EVALUATION OF A HUMAN PANCREAS-SPECIFIC ANTIGEN (MEETING ABSTRACT).

Loor R, Kuriyama M, Shimano T, Manzo ML, Inaji H, Douglass HO, Berjian R, Nicolai JJ, Tytgat GN, Chu TM
Roswell Park Memorial Institute, Buffalo, NY
Newsletter Natl Pancreas Cancer Project; VI(2):36 1981

A pancreas-specific antigen (PaA) has been identified by immunologic techniques and purified from saline extract of human pancreas. The purified PaA has a mol wt of 44,000 and a sedimentation coefficient of 3.4S. PaA possessed an isoelectric point of 4.9 and migrated to alpha-beta region upon immunoelectrophoresis. Immunochemical staining revealed that PaA was located in acinar cells of human p ancreas. In addition a higher concentration of PaA was detected in pancreatic juice than in the saline extract of pancreas. A sensitive and reproducible sandwich-type enzyme immunosorbent assay has been developed for quantitation of PaA. With this method, PaA at a concentration as low as 0.8 ng/ml can be detected. Serum PaA levels from 51 healthy persons ranged from less than 4 to 34 ng/ml. Using 21.5 ng/ml (the upper 97.5 percentile of normal controls) as an upper limit, 50 of 76 pancreatic cancer (66%), 4 of 16 pancreatitis (25%) and 3 of 8 cholelithiasis (38%) had an elevated PaA. Among 16 pancreatitis patients, 3 of 6 (50%) acute pancreatitis and 1 of 10 (10%) chronic pancreatitis patients had an elevated PaA level. In 76 pancreatic cancers, 6 of 10 (60%) stage I, 11 of 18 (61%) stage II, and 33 of 48 (69%) stage III pancreatic cancer patients showed an elevated PaA level. Very few patients with other cancers, however, were shown to have an elevated PaA; 4/56 (7%) of lung cancer, 2/50 (4%) of colorectal cancer, 4/49 (8%) of prostate cancer and 1/39 (3%) of breast cancer. The sensitivity and specificity of serum PaA test for the detection of pancreatic cancer were calculated to be 66% and 95%, respectively. PaA was detected in pancreatic carcinoma by immunocytochemical technique. These results indicate that PaA may be useful as an adjunctive tool in immunodiagnosis of pancreatic cancer. (no Refs)

6. RADIOIMMUNE ASSAY STUDIES OF SERUM AND ASCITES FROM PANCREATIC CANCER PATIENTS FOR AN ANTIGEN (DU-PAN-2) DETECTED BY A MONOCLONAL ANTIBODY (MEETING ABSTRACT).

Daasch VN, Metzgar RS
Department of Microbiology and Immunology, Duke University Medical Center, Durham, NC, 27710
Newsletter Natl Pancreas Cancer Project; VI(2):18 1981

DU-PAN-2 monoclonal antibodies detect an antigen that appears to be a glycoprotein with the antigenic determinant in the carbohydrate portion of the molecule. Treatment of reactive cells with neuraminidase destroys antigenic activity. An inhibition radioimmune assay was developed to detect soluble DU-PAN-2 antigen in body fluids of patients with various malignancies, including pancreatic adenocarcinoma. Patient ascitic fluid or serum was preincubated with the DU-PAN-2 antibody; the mixture was then allowed to react with crude soluble antigen extracted from pancreatic tumor tissue culture cell lines, or spent medium from the cultures. DU-PAN-2 antibody bound to crude antigen was detected with 125I labeled goat antimouse Ig. Strong inhibitory activity (greater than 85% inhibition) was observed in the ascitic fluid of the patient from which the immunizing cell line (HPAF) was derived. Significant inhibition (40 to 90%) was also noted in ascites from another pancreatic tumor patient as well as in ascites from patients with certain other types of carcinomas. Many ascitic fluids from non-pancreatic malignancies as well as ascites from patients with non-malignant disease demonstrated little or no blocking activity. Blocking antigen activity was also detected in a fractionated serum of a patient with advanced metastatic pancreatic cancer as well as in sera of other cancer patients. Fractionated sera from normal volunteers or leukemic patients showed little or no inhibition. (no Refs)

7. ISOLATION AND CHARACTERIZATION OF AN ANTIGEN FROM PANCREAS CARCINOMA IMMUNE COMPLEXES (MEETING ABSTRACT).

Campagnari T, Howell JH, Douglass HO, Goldrosen MH
Department of Surgical Oncology, Roswell Park Memorial Institute, Buffalo, New York, 14263
Newsletter Natl Pancreas Cancer Project; VI(2):14 1981

To date, effusion fluid from 8 patients with pancreatic cancer have been fractionated in order to obtain pancreas tumor antigen(s). Immune complex antigen was obtained by sequential ammonium sulphate precipation, S-300 column chromatography, protein A chromatography and preparative isoelectric focusing (IEF). Potassium bromide flotation of unique low isoelectric point (pI) material yielded two fractions. Analytical gel IEF of the lipid fraction indicated that it had a pI of 3.3 while the non-lipid fraction had a pI of 2.6. Polyacrylamide gel electrophoresis in sodium dodecyl sulphate with B-mercaptoethanol of the non-lipid fraction yielded two coomasie blue staining bands. One has mol wt of 67,000 daltons while the other has a mol wt of 15,000 daltons. Five of the 8 pancreatic effusion fluids contain this acidic non-lipid molecule. Xenogeneic antisera to the acidic molecule raised in a goat by established procedures demonstrated precipitating antibody by Ouchterlony analysis to all but the two malignant effusion fluids that did not contain the acid material with a pI of 2.6. Three control effusion fluids did not contain the acidic material, and no immunologic recognition was observed with the goat antisera by Ouchterlony analysis. Thus, immune complexes from pancreatic malignant effusion fluids contain an antigen(s) with a pI of 2.6. These acidic antigen(s) will be further characterized by immunologic and biochemical criteria. (no Refs)

8. HUMAN MELANOMA-ASSOCIATED ANTIGENS; IMMUNOCHEMICAL AND MOLECULAR PROFILE.

Reisfeld RA, Galloway DR, Morgan AC, Walker LE, Bumol TF

Scripps Clinic and Res. Foundation, La Jolla, CA

Cancer Bull; 33(5):211-218 1981

Some of the immunochemical approaches taken in the authors' laboratory to isolate and characterize two human melanoma-associated antigens utilizing specific polyclonal and monoclonal antibodies are described. Analysis of cellular proteins released into the surrounding culture of several human melanoma cells lines indicated three major components detected by polyclonal antimelanoma xenoantisera with mol wt of 260K (260,000), 240K and 100K. The 240K component has been identified as fibronectin. The 100K component is found in spent media of both melanoma and carcinoma cell lines. The 100K and 260K dalton antigens which have affinity for specific lectins and metabolic radiolabeling with sugars strongly suggest they were glycoproteins. Other studies are reported on the use of monoclonal antibody for structural characterization, production of monoclonal antibody, subunit composition of 100K and 250K dalton melanoma antigens, and functional properties. It is apparent that the two melanoma-associated antigens of 100K and 250K dalton, defined immunochemically by monoclonal antibody, are likely to play a key role in the elicitation of host immune responses to malignant melanoma. Furthermore, it appears that changes in intracellular transport, glycosylation, and cell-surface expression of these two markers may be associated with neoplastic transformation. (12 Refs)

9. SURFACE ANTIGENS OF HUMAN MELANOMA CELLS DEFINED BY MONOCLONAL ANTIBODIES. I. BIOCHEMICAL CHARACTERIZATION OF TWO ANTIGENS FOUND ON CELL LINES AND FRESH TUMORS OF DIVERSE TISSUE ORIGIN.

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Institut fur Immunologie, Schillerstr. 42, D-8000 Munchen 2, W. Germany

Eur J Immunol; 11(10):825-831 1981

Monoclonal antibodies were produced against melanoma cell lines derived from patients presently disease free. Based on tissue distribution of binding, the antibodies obtained could be used to classify melanoma surface antigens into groupings similar to those obtained from studies of autologous and xenogeneic antibodies. Three antibodies (21.43, 15.75 and 15.95) reacted with the immunizing tumor but not with peripheral blood lymphocytes or a lymphoblastoid cell line derived from the tumor donor. When tested on a broader cell panel, antibody 21.43 reacted only with melanoma lines, while antibodies 15.75 and 15.95 reacted with carcinoma cell lines as well as with the majority of melanoma cell lines. Antibody 15.95 precipitated a 49,000 dalton glycoprotein from both melanoma and carcinoma cells. Antibody 15.75 precipitated a 74,000 dalton glycoprotein from the surface of melanoma and carcinoma cell lines which is also found on freshly isolated tumor cells from melanoma and carcinoma metastases in vivo. (Author abstract) (30 Refs)

10. PURIFICATION OF ANTIGENS FROM URINE OF A SARCOMA PATIENT BY AFFINITY CHROMATOGRAPHY.

Huth JF, Gupta RK, Morton DL
(c/o Morton), Univ. California, 54-140 CHS, Los Angeles, CA, 90024
J Surg Oncol; 18(3):237-247 1981

Antigens are present in the urine of cancer patients, detectable by the complement fixation (CF) assay. Development of methodology for purification of these tumor-associated antigen(s) using xenogeneic antisera as a specific immunoabsorbent is presented. Urine possessing high antigen titer was collected from sarcoma patients. Xenoantiserum to the urinary antigens was prepared by injection of concentrated, dialyzed urine mixed with complete Freund's adjuvant into rabbits. The antisarcoma urine xenoantisera were absorbed with human normal liver and insolubilized human normal serum to remove cross-reacting antibodies to normal human components. The Ig fraction of the xenoantisera was isolated by ammonium sulfate precipitation and covalently linked to Sepharose 4B beads. Urine from a sarcoma patient was reacted with the immunobeads, and the affinity absorbed antigen(s) were eluted with 3.5 M potassium thiocyanate. The affinity purified urinary antigen had a CF titer of 1:128 against xenoantisera that had been quantitatively absorbed with human normal liver cells and the insolubilized normal human serum. Absorption of the xenoantiserum with cultured allogeneic sarcoma cells removed all activity against the affinity purified antigen(s). The results suggest that the cultured sarcoma cells expressed antigens immunologically similar to those present in the urine of sarcoma patients, and that these antigens can be isolated from urine of cancer patients and purified by affinity chromatography. By radioimmunoassay, antisarcoma urine xenoantiserum absorbed with human normal liver and insolubilized serum had a titer of 1:4,000 against the affinity purified antigen. Xenoantisera to pooled normal human urine treated similarly showed no reactivity to the affinity purified antigen. Polyacrylamide gel electrophoresis of the radiolabeled antigen(s) showed a single peak in the 40,000-to 50,000-dalton range. (25 Refs)

11. TUMOUR-ASSOCIATED ANTIGENS REACTING WITH CYTOTOXIC ANTIBODIES IN SERUM OF HEPATOMA-BEARING RATS.

Lando P, Berzins K, Gabriel J, Larsson P, Perlmann P
Dept. Immunology, Univ. Stockholm, S-10691 Stockholm, Sweden
Br J Cancer; 44(4):522-531 1981

The 3M-KC1 extracts of the hepatoma D23 contain antigens that inhibit the complement-dependent cytotoxicity for D23 hepatoma cells of serum from D23 tumor-bearing rats (D23 TBS). Inhibition was not due to a general anticomplementary activity of the extracts. Although a minor part (25%) of the protein of D23-KC1 extract was insoluble in PBS, this part contained most of the inhibitory activity. Fractionation of the PBS-soluble material of the extract on Concanavalin A-Sepharose showed that the inhibitory activity did not bind to the lectin. Analysis of D23-KC1 extracts on a Sepharose CL-4B column showed that the antigens involved in the cytotoxicity were heterogeneously distributed in the high-mol wt region (greater than 200,000). Precipitation with 10% trichloroacetic acid (TCA) of D23 KC1 extracts revealed that most of the antigenicity was insoluble in TCA. Heating of D23 KC1 extracts at 100 C did not affect the antigenicity. Enzyme treatment of D23 extra nuclear membranes (D23 ENP) revealed that the inhibitory activity was not sensitive to proteolytic digestion, while treatment with phospholipase A2, C or D abrogated partly the inhibitory activity. The lipid nature of the antigenicity was indicated by its solubility in organic solvents as chloroform or n-butanol. (Author abstract) (25 Refs)

12. COMPARISON OF T ANTIGEN-ASSOCIATED HOST PHOSPHOPROTEINS FROM SV40-INFECTED AND -TRANSFORMED CELLS OF DIFFERENT SPECIES.

Fanning E, Burger C, Gurney EG
Fakultat fur Biologie, Universitat Konstanz, D-7750 Konstanz, W. Germany
J Gen Virol; 55(part2):367-378 1981

Simian virus 40 (SV40)-infected and -transformed cells contain, in addition to the virus-coded tumor antigens, one or more 48K to 56K host tumor antigens. At least part of this class of host proteins exists as a fast-sedimenting complex with the SV40 large T antigen. The host proteins associated with the large T antigen in SV40-transformed monkey, mouse and human cells and SV40-infected monkey cells were compared by two-dimensional gel electrophoresis and V8 partial proteolysis peptide mapping. Although these proteins differed slightly in apparent mol wt and peptide pattern, they migrated identically in isoelectric focusing gels. These results suggest that the cellular proteins associated with large T antigen in different hosts are very closely related to each other. Despite their similarities, the 55K proteins from different host cells form complexes of different stabilities with large T antigen, as judged by spontaneous dissociation of the complexes during storage, and the fractions of the 55K cellular protein and large T antigen found free and in the complexed form in each different host cell. (Author abstract) (36 Refs)

13. RED BLOOD CELLS COATED WITH TUMOR CELL EXTRACTS AS TARGETS IN 51CR RELEASE ASSAYS.

Karjalainen HE, Mantyjarvi RA
Dept. Clinical Microbiology, Univ. Kuopio, POB 138, SF-70101 Kuopio 10, Finland
Acta Pathol Microbiol Scand [C]; 89(4):315-319 1981

Sheep RBC were coated with tumor cell antigens prepared by extractions with 3M KCl. The coated cells were labelled with 51Cr and used as targets in immuno-assays. The technique was found suitable for complement-mediated as well as antibody-dependent cell-mediated reactions, and it offers several applications for use in tumor immunology. (Author abstract) (35 Refs)

IMMUNOLOGICAL STUDIES

14. ISOLATION OF LUNG CARCINOMA-ASSOCIATED ANTIBODIES FROM IMMUNE COMPLEXES AND PRODUCTION OF HETEROLOGOUS ANTISERA.

Cronin WJ, Dorsett BH, Ioachim HL
(c/o Ioachim) Dept. Pathology, Lenox Hill Hosp., 0 East 77th St., New York, NY, 10021
Cancer Res; 42(1):292-300 1982

Immune complexes isolated from pleural effusions of lung carcinomas were dissociated by ion exchange chromatography in the presence of 8 M urea. The antibodies thus obtained from two lung adenocarcinomas and two squamous cell carcinomas were assayed by indirect immunofluorescence against a variety of target cells in fresh suspensions, tissue cultures, and paraffin-embedded sections. Strong cytoplasmic fluorescence was obtained with greater than 90% of the cell populations of all major histological types of lung carcinomas, and negative fluorescence was obtained with the cells of normal lung tissues and most of the nonpulmonary carcinomas. Antigen fractions prepared from the same lung carcinoma-associated immune complexes were used to immunize rabbits for the production of antisera directed against human lung carcinoma. The rabbit antibody preparations after proper absorptions were assayed in indirect immunofluorescence showing patterns of reactivity with normal and tumor cells of various derivations similar to those obtained with the human antibodies. Complete blocking of immunofluorescence staining with both allogeneic and xenogeneic antibody preparations was achieved by prior absorption with lung tumor tissue extracts or with various lung tumor antigen preparations. The present study demonstrates the isolation from lung tumor effusion immune complexes of antibodies with high affinity for lung carcinoma cells and of antigens that can be used to produce tumor-directed heterologous antibodies. The immunofluorescence staining of lung carcinoma-associated antigens in situ on paraffin-embedded sections provides new, topographical information. (Author abstract) (43 Refs)

15. IMMUNOCHEMICAL AND IMMUNOCYTOCHEMICAL LOCALIZATION OF S-100 ANTIGEN IN NORMAL HUMAN SKIN.

Cocchia D, Michetti F, Donato R
Dept. Anatomy, Universita Cattolica, Roma 00168, Italy
Nature; 293(5836):85-87 1981

The presence of S-100 antigen in normal human skin is reported. Levels of S-100 were measured by microcomplement fixation assay in normal skin and in human melanomas using a specific antibody raised against ox S-100. The amounts of S-100 were measured in samples containing 15 or 25 ug total protein; no appreciable anticomplementary activity was observed. The S-100 antigen was detected in measurable amounts in both the normal skin (0.03 ug/mg soluble protein) and melanoma (1.90 ug/mg soluble protein). In normal epidermis, S-100 reaction product was detected by electron microscopy (using the unlabelled antibody Papanicolaous's test with the same antiserum) in the perikarya and in the cytoplasmic processes of both melanocytes and Langerhans cells. No reaction production was present in the keratinocytes of any epidermal layer. In normal dermis, S-100 reaction product was detected not only in typical Langerhans cells, but also in cells with ultrastructural features comparable with Langerhans cells but lacking the characteristic granules. The results indicate that definite cutaneous cell types normally contain significant amounts of S-100 antigen, but at a much lower concentration than in malignant tissue. (22 Refs)

16. IMMUNOPEROXIDASE STUDIES ON A TUMOR-CELL-ASSOCIATED ANTIGEN(S) IN RAT RENAL NEOPLASMS INDUCED BY DIMETHYLNITROSAMINE.

Yantchev IK
Inst. General and Comparative Pathology, Bulgarian Acad. Sciences, Sofia-1113, Bulgaria
Neoplasma; 28(4):447-455 1981

Renal neoplasms were induced in rats of Wistar line by a single, ip injection of dimethylnitrosamine (60 mg/kg). The histological investigation indicated that these tumors were entirely mesenchymal in nature. In some of them (16.6%) small adenocarcinomas were seen. Immunological studies were carried out by light and electron microscope, using the immunoperoxidase 'bridge' technique. Tumor cell-associated antigen(s) was detected in 62% of the neoplasms examined. This antigen was individual as it did not react with sera from the other tumor bearing rats. It was established that this antigen was located mainly on the plasma membrane and also, even though in a lesser degree, on the endoplasmic reticulum and nuclear envelope of the tumor cells of mesenchymal and epithelial origin. Except the existence of tumor cell-associated antigen(s) in these neoplasms, the presence of antibodies produced against them in the sera of the diseased rats were also detected by these investigations. (Author abstract) (23 Refs)

17. INCREASED EXPRESSION OF IA ANTIGENS ON THYMOCYTES FROM LATE PRELEUKEMIC AND LEUKEMIC ARK MICE.

Zielinski CC, Datta SK, Waksal SD
Cancer Res. Center, 136 Harrison Ave., Boston, MA, 02111
Immunogenetics; 14(1/2):169-176 1981

Thymocyte Ia-antigen levels in AKR mice and 'low leukemia' control mice [C3H, CBA, and (AKR x NZB)F1] were analyzed with the use of fluorescent monoclonal antibodies and a fluorescence-activated cell sorter. The percentage of Ia-expressing thymocytes in AKR mice increased markedly in the late preleukemic and leukemic stages, compared with the percentage in thymocytes from young and early preleukemic mice and the control strains. Nine of 10 late preleukemic and 9/11 leukemic AKR mice showed increased Ia antigen expression that correlated temporally with an increase in thymocyte levels of murine leukemia virus antigens. (30 Refs)

VIRUS ASSOCIATED ANTIGENS

18. IDENTIFICATION OF ANTIGENIC DETERMINANTS UNIQUE TO THE SURFACES OF CELLS TRANSFORMED BY EPSTEIN-BARR VIRUS.

Kintner C, Sugden B
Div. Biology, California Inst. Technology, Pasadena, CA, 91125
Nature; 294(5840):458-460 1981

Four monoclonal antibodies (anti-EBVCS) that detect antigenic determinants unique to the surfaces of Epstein-Barr virus (EBV)-transformed cells but are not associated with virus production were isolated. Cell lines transformed in vitro or those transformed in vivo but not associated with Burkitt's lymphoma bound anti-EBVCS strongly, whereas cell lines from patients with Burkitt's lymphoma bound them at intermediate levels or not at all. When untreated lymphocytes and lymphocytes exposed to EBV, Concanavalin A, and pokeweed mitogen were assayed, only EBV-exposed lymphocytes expressed EBVCS determinants, which were detectable within 48 hr after infection. Assay of unseparated populations of EBV-exposed primary lymphocytes and immunoglobulin-positive and -negative populations indicated that those cells which express EBVCS determinants are separated as B cells along with those which express the EBV-induced nuclear antigen and that the two antigen-expressing populations are overlapping and may be identical. A polypeptide with an apparent mol wt of 45,000 was precipitated from an EBVCS-positive cell line and was likely to be the molecule which carries EBVCS determinants. The results indicate that EBVCS determinants are expressed at reduced levels on cell lines established from Burkitt's lymphoma patients relative to expression on other EBV-transformed cell lines. EBVCS determinants are among possible determinants recognized by autochthonous, cytotoxic T cells specific for EBV-transformed cells and may therefore be equivalent to lymphocyte determined membrane antigen (LYDMA); this possibility was supported by the finding that EBVCS and LYDMA were expressed with the same time course in lymphocytes infected with EBV in vitro. If the EBVCS determinants are used by cytotoxic T cells to identify their targets, reduced expression of EBVCS on Burkitt's lymphoma cell lines is consistent with these tumor cells having been selected in vivo to survive that cytotoxic response. (18 Refs)

19. A GEOGRAPHICAL STUDY OF ANTIBODIES TO MEMBRANE ANTIGENS OF HSV-2-INFECTED CELLS AND HSV-2-SPECIFIC ANTIBODIES IN PATIENTS WITH CERVICAL CANCER.

Mendis LN, Best JM, Senarath L, Chiphangwi J, Vestergaard BF, Banatvala JE
Dept. Microbiology, Faculty of Medicine, Post Office Box 271, Kynsey Road, Colombo 8, Sri Lanka
Int J Cancer; 28(5):535-542 1981

Sera were obtained from patients with squamous carcinoma of the cervix from Great Britain (29), Sri Lanka (32), Malawi (27) and Sudan (27), and from controls from all countries except Sudan. Controls were matched for ethnic origin, age and social class. Sera were tested by indirect immunofluorescence (IF) for IgG and IgA antibodies to membrane antigens (MA) and IgA antibodies to VCA of HSV-2 infected cells. Compared with controls, IgA antibodies to MA (IgA anti-MA) were detected more frequently and at higher titers in all groups of patients. However, there was no significant difference in prevalence of these antibodies at titers greater than or equal to 1:4 between Malawian patients and controls, although a significantly higher proportion of patients had IgA anti-MA titers of greater than or equal to 1:16. In contrast, I gA anti-VCA did not distinguish patients from controls. More than 90% of both patients and controls from all countries had IgG antibodies to MA (IgA anti-MA). Malawian patients had a significantly higher geometric mean titer (GMT) of IgG anti-MA than controls and both patients and controls had significantly higher GMTs than their counterparts from other countries. The variation between herpes IgG anti-MA titers in subjects from different countries did not reflect differences in serum Ig levels and similar variations in titer were not seen in rubella and measles HAI titers. Among the patients there was a geographical variation in the prevalence of HSV-2 specific antibodies detected by ELISA, which varied from 52% among British and Sudanese patients to 73% among Malawian patients. Even when adjustment was made for possible false negative results, there were between 10 and 31% patients without HSV-2-specific antibodies, although only 2 of 103 (1.9%) patients had neither HSV-1 nor HSV-2 antibodies. The association of HSV-2 with cervical carcinoma appeared to vary with age. (Author abstract) (52 Refs)

20. HERPESVIRUS ANTIGENS AS MARKERS FOR CERVICAL CANCER.

Gupta PK, Aurelian L, Frost JK, Carpenter JM, Klacsmann KT, Rosenshein NB, Tyrer HW
Dept. Pathology, John Hopkins Univ. Sch. Medicine, Baltimore, MD, 21205
Gynecol Oncol; 12(2,part2):S232-S258 1981

A total of 393 patients representing cervical atypias, cancers, and nonneoplastic disease have been studied. Cellular specimens have been stained with antisera raised against total herpes Type 2 virus (HSV-2) and subfractions labeled crude AG-e, pure AG-e, ICP 12, and ICP 14. Reproducibility, statistical significance, false positive and false negative results, specificity, and sensitivity of the various antisera have been investigated. Correlation of immunocytostaining with Papanicolaou staining has been made. Usefulness of these markers in the detection and diagnosis of premalignant and malignant cervical epithelial changes for mass screening has been discussed. Using crude AG-e, pure AG-e, HSV-2, and HSV-1 antisera in a number of blind studies, no significant differences were found in the reproducibility of results. Observations indicated that a minimum of 30 cells must be analyzed to make data amenable to statistical analysis. Exfoliated cells from 62, 75, 77, and 94% of patients respectively diagnosed as mild, moderate, and marked atypia, and cancer were studied with antisera against total HSV-2. Similar results were observed with antisera against pure AG-e. No patient reacted with anti-AG-e or anti-HSV-1 antiserum in the absence of reactivity to antisera against total HSV-2 antigens. Studies using anti-ICP 12 and -ICP 14 antigens established the wide and specific staining character of anti-HSV-2 antisera. Morphologic preservation of cells by Papanicol aou staining after the FA procedures was considered satisfactory for diagnostic purposes. Our studies indicated the potential usefulness of anti-HSV-2 and anti-AG-e antisera in mass cervical cancer screening programs and cytology automation. (Author abstract) (21 Refs)

21. CONVERSION OF HERPETIC LESIONS TO MALIGNANCY BY ULTRAVIOLET EXPOSURE AND PROMOTER APPLICATION.

Burns JC, Murray BK
Dept. Oral Pathology, Dept. Microbiology, Medical Coll. Virginia, Virginia Commonwealth Univ., Richmond, VA, 23298
J Gen Virol; 55(part2):305-313 1981

Many lines of evidence exist associating herpes simplex virus (HSV) with the development of carcinoma, but much of this evidence is anecdotal or associative in nature and does not prove a cause and effect. The purpose of this research was to investigate the oncogenic potential of HSV Type 2 (HSV-2) in vivo. A mouse model for lip carcinogenesis was designed to combine HSV-2 infection, UV exposure and tetradecanoylphorbol-acetate (TPA) application. HSV-2 inoculation on to abraded mouse lips was capable of causing vesicular ulcerative lesions which healed completely after 10 to 14 days. UV irradiation of the HSV lesion site daily for 6 min at 42 ergs/mm2/s on days 3 to 6 post-infection caused hyperkeratosis, acanthosis and dysplasia to develop in several lips; while the same UV exposure by itself failed to alter the histologic appearance. The addition of repeated TPA application to the HSV + UV regimen promoted tumor emergence. Thirty-two of 156 Balb/c mice developed tumors. Although the majority were papillomas, six were squamous cell carcinomas. These tumor-bearing mice had increased HSV-specific antibody titers. HSV antigens were shown to be present in outgrowths from explanted tumors as well as in tumor biopsies by immunoperoxidase staining with HSV-specific antisera. It is suggested that the in vivo UV-irradiated HSV acted as an inducer and TPA as the promoter, analogous to the classical two-stage carcinogenesis model. (Author abstract) (29 Refs)

22. LIVER CELL DYSPLASIA IN ASSOCIATION WITH HEPATOCELLULAR CARCINOMA, CIRRHOSIS AND HEPATITIS B SURFACE ANTIGEN IN HONG KONG.

Ho JC, Wu PC, Mak TK
Dept. Pathology, Univ. Hong Kong, Hong Kong, China
Int J Cancer; 28(5):571-574 1981

Liver-cell dysplasia was identified in 60% of 558 cases of cirrhosis with and without hepatocellular carcinoma (HCC) in Chinese coming to necropsy in Hong Kong from 1963 to 1978. A significant correlation was found between liver-cell dysplasia and the identification of hepatitis B surface antigen (HBsAg) in the livers, suggesting that dysplasia may be causally related to hepatitis B virus (HBV). Applying Bayes' theorem to our series of male deaths, we calculated that for Chinese male non-cirrhotics showing liver-cell dysplasia at necropsy, compared with male non-cirrhotics showing no liver-cell dysplasia, the approximate risk factor for HCC is 13:1, whereas for male cirrhotics with liver-cell dysplasia, compared with male cirrhotics without liver cell dysplasia, the risk factor for HCC is approx 2:1. In the presence of dysplasia, the risk for HCC is increased two-fold in males who are also HBsAg-positive. Thus, the presence of liver-cell dysplasia in cirrhotic or non-cirrhotic livers accompanies a significantly higher risk of developing HCC, especially in the presence of HBsAg. (Author abstract) (10 Refs)

23. EVIDENCE FOR PAPILLOMAVIRUS GENUS-SPECIFIC ANTIGENS AND DNA IN LARYNGEAL PAPILLOMA.

Lancaster WD, Jenson AB
Dept. Surgery, Univ. Hosp., 2065 Adelbert Road, Cleveland, OH, 44106
Intervirology; 15(4):204-212 1981

Four juvenile laryngeal papillomas (JLPs) were examined for papillomavirus genus-specific structural antigens and polynucleotide sequences employing reagents derived from bovine papillomavirus Type 1 (BPV-1). Three of four JLPs contained intranuclear antigens in the granular layer of differentiating epithelial cells of formalin-fixed, paraffin-embedded papillomas assayed by the peroxidase-antiperoxidase reaction using an antiserum prepared against purified detergent-disrupted BPV-1. Examination of these JLPs for viral sequences indicated two tumor DNA preparations contained polynucleotide sequences which hybridized to an in vitro labeled BPV-1 DNA probe under nonstringent conditions. These sequences were detectable after gel electrophoresis and immobilization of restriction-endonuclease-digested JLP DNAs onto nitrocellulose membranes. Specific hybridization of probe to digested JLP DNA was visualized as bands in autoradiograms coincidental with open circular and linearized papillomavirus DNA. Hybridization was extensively reduced when JLP DNA preparations were prehybridized to an unlabeled papillomavirus DNA heterologous to the probe. These results provide direct evidence for the association of a papillomavirus in JLP. (Author abstract) (32 Refs)

24. RELATIONSHIP OF THE FELINE ONCORNAVIRUS ASSOCIATED CELL MEMBRANE ANTIGEN TO A FELINE SARCOMA VIRUS ENCODED POLYPROTEIN.

Snyder HW, Dutta-Choudhury M, Hardy Jr WD
No affiliation given
Haematol Blood Transfus; 26:488-491 1981

Using immunoaffinity chromatography on a column of Sepharose containing bound IgG from cat anti-feline oncornavirus-associated cell membrane antigen (FOCMA) serum, a 70,000-dalton protein was isolated from lysates of mink cells transformed by the Gardner-Arnstein strain of feline sarcoma virus (GA-FeSV). This result was unanticipated because previous evidence had suggested that FOCMA was associated with the much larger (95,000 dalton) gag-x fusion protein in these cells. The GA-FeSV gag-x protein was also isolated by virtue of its binding to anti-FeSV antibodies on a different affinity column. Preliminary biochemical characterization of the 70,000-dalton protein from both GA-FeSV-transformed mink fibroblasts and feline lymphosarcoma cells showed no differences between them. The gag-x protein was distinguishable by labelling with 32P-orthophosphate, association with protein kinase activity, and its precipitation ability with antibodies in a hyperimmune antiserum to FeLV structural proteins. It is hypothesized that FOCMA may actually be a family of antigens, not all of which cross-react with FeSV polyprotein antigens. (21 Refs)

25. ONCOGENIC ACTIVITY OF THE BK TYPE OF HUMAN PAPOVA VIRUS IN NEWBORN WISTAR RATS.

Noss G, Stauch G, Mehraein P, Georgii A
Institut fur Virologie und Seuchenhygiene, Medizinische Hochschule Hannover, Karl-Wiechert-Allee 9, D-3000 Hannover 61, W. Germany
Arch Virol; 69(3/4):239-251 1981

The oncogenic potential of the human papova virus BK (= BKV) has been examined in newborn Wistar rats. Twelve of 37 animals inoculated with BKV sc and 7 of 40 animals inoculated with BKV ic developed tumors of various histological types. The latency periods ranged from 6 to 18 mo. The BKV etiology of tumors was supported by detection of BKV T antigen in cells of established tumor lines by means of indirect immunofluorescence. No tumors appeared in animals given injections of saline instead of virus. BKV T antibodies were detected in sera of 100% of animals bearing tumors but not in sera of control animals. Only 3 of 77 BKV infected and none of the control animals developed spontaneous tumors (adenomas). (Author abstract) (16 Refs)

26. LOCALIZATION OF THE ABELSON MURINE LEUKEMIA VIRUS PROTEIN IN A DETERGENT-INSOLUBLE SUBCELLULAR MATRIX: ARCHITECTURE OF THE PROTEIN.

Boss MA, Dreyfuss G, Baltimore D
Center for Cancer Res., Dept. Biology, Massachusetts Inst. Technology, Cambridge, MA, 02139
J Virol; 40(2):472-481 1981

We examined the interaction of Abelson murine leukemia virus protein P120 with other cellular components after extraction with the nonionic detergent Triton X-100. Most of the Abelson murine leukemia virus P120-associated kinase activity was found in the detergent-insoluble matrix in both lymphoid and fibroblast cell lines. The P120 labeled during a short exposure of cells to [35S]methionine was mainly in the detergent-insoluble matrix (lymphoid cells) or equally distributed in the detergent-insoluble matrix and the soluble fraction (fibroblasts). Steady-state-labeled P120 was distributed equally in the two fractions (lymphoid cells) or mostly in the soluble portion (fibroblasts). Thus, there was an apparent movement of P120 from the detergent-insoluble matrix to the detergent-soluble fraction and a concomitant loss of enzymatic activity. When the detergent-insoluble matrix was incubated with [32P]ATP in situ, phosphorylation of tyrosine residues of P120 was observed. We found an 80,000-mol-wt fragment of P120 (designated F80) after extraction of fibroblast cells with detergent. F80 was not found in extracted lymphoid cells, but mixing labeled lymphoid cells and unlabeled fibroblasts before extraction produced the fragment. F80 contained the gag determinants of P120 but did not react with Abelson-specific serum. These data allowed us to assign various features of the protein to regions of the P120 molecule and to localize the Abelson-specific antigenic determinants to the C-terminal region of the molecule. (Author abstract) (29 Refs)

27. DIFFERENTIAL EXPRESSION OF MURINE LEUKEMIA ANTIGEN ON L1210 PARENTAL AND DRUG-RESISTANT SUBLINES.

Strzadala L, Opolski A, Radzikowski C, Mihich E
Inst. Immunology and Experimental Therapy, Czerska 12, 53-114, Wroclaw, Poland
Cancer Res; 41(12):4934-4937 1981

The differential expression of surface antigens on L1210 leukemia DBA/2 and drug-resistant L1210 sublines was investigated. In direct cytotoxic test, the anti-L1210/v alloantiserum reacted more strongly with subline cells than with parental cells. Absorption of the antiserum with Gross cellular surface antigen-positive AKR leukemia (AKSL-4) cells led to a much greater difference in this reactivity. Quantitative absorption experiments revealed that the drug-resistant sublines had 5x higher absorption capacity than did the parental line. After complete absorption of antibodies against murine leukemia virus-related antigens, the anti-L1210/v alloantiserum still reacted with L1210 cells. This cytotoxicity could be removed after absorption with C3H mammary tumor (MAC-1) cells but not with normal C3H lymphocytes. These results provide evidence that the major cytotoxic activity of the antiserum against L1210 and L1210 subline cells was due to antibodies against murine mammary tumor virus-related antigen and that the drug-resistant sublines of leukemia L1210 have higher quantitative expression of mammary leukemia antigens. (Author abstract) (15 Refs)

28. NONLYTIC SIMIAN VIRUS 40-SPECIFIC 100K PHOSPHOPROTEIN IS ASSOCIATED WITH ANCHORAGE-INDEPENDENT GROWTH IN SIMIAN VIRUS 40-TRANSFORMED AND REVERTANT MOUSE CELL LINES.

Chen S, Verderame M, Lo A, Pollack R
Dept. Biological Sciences, Columbia Univ., New York, NY, 10027
Mol Cell Biol; 1(11):994-1006 1981

The two distinct growth controls of normal fibroblasts can be assayed as requirements for serum or anchorage. Interaction of mouse 3T3 fibroblasts with simian virus 40 (SV40) generates four lines of transformed (TR) cells (fully TR, anchorage TR, serum TR and fully reverted). Viral gene expression was studied in these four lines. Immunoprecipitation of (35S)methionine labeled cell extracts with an antiserum from tumor-bearing hamsters detected the SV40 large T and small t proteins (94,000 mol wt [94K], 17 K) and the nonviral host 54K protein in all four lines. A 100K tumor antigen was found in some, but not all lines; similar molecules have been reported in many rodent transformed lines. Analysis of the relation of phenotype to relative amounts of the various proteins in the cell classes, using the Spearman rank correlation test, showed the amount of 100K T antigen relative to 94K T antigen or to total viral protein correlated well with ability to form colonies in semisolid medium. No significant correlation was found between quantities of labeled 94K T antigen, 54K host antigen, or 17K t antigen and either serum or anchorage independence. Mouse cell TR with small t SV40 deletion mutant 884 synthesized a 100K T antigen, suggesting small t is not required. The 100K T antigen migrated more slowly than the lytic T. It is concluded that since mixtures of extracts from cells expressing and lacking the 100K T antigen yielded the expected amount of this protein, it is unlikely that the 100K T derives from the 94K protein by a posttranslational modification. (70 Refs)

29. HANGANUTZIU AND DEICHER TYPE HETEROPHILE ANTIGEN EXPRESSED ON THE CELL SURFACE OF MAREK'S DISEASE LYMPHOMA-DERIVED CELL LINES.

Ikuta K, Kitamoto N, Shoji H, Kato S, Naiki M

Dept Pathology, Research Inst. Microbial Diseases, Osaka Univ., Suita, Osaka 565, Japan

Biken J; 24(1/2):23-27 1981

Antibodies to Marek's disease (MD) tumor-associated surface antigen (MATSA) were prepared by immunizing chickens with the MSB1 lymphoblastoid cell line derived from an MD lymphoma. All the chicken anti-MSB1 sera examined contained heterophile antibodies, which agglutinated sheep RBC (SRBC) and were absorbed with bovine RBC (BRBC) or the precipitate of a guinea pig kidney homogenate. Their heterophile properties were identical with those of Hanganutziu and Deicher (H-D) heterophile antibodies in humans. The heterophile antibodies were also stimulated in chickens, even when the MSB1 cells cultured in medium containing homologous chicken serum instead of the heterologous fetal calf serum were used for immunization. H-D antigenic molecules were previously purified from equine and bovine RBC as the hematoside N-glycolylneuraminyl lactosyl ceramide and ganglioside N-glycolylneuraminyl lactneotetraosyl ceramide, respectively. Both glycosphingolipids specifically diminished the heterophile activity of chicken anti-MSB1, but did not completely inhibit MATSA activity. For demonstration of the specific expression of H-D antigen on MD tumor-derived cell lines, the antibodies to the two glycosphingolipid antigens and SRBC were prepared in chickens by immunization. The antibodies of anti-hematoside and anti-SRBC were purified with BRBC stroma as immunoadsorbent. These antisera and the purified antibodies cross-reacted with both the glycosphingolipids, but not with another ganglioside (GM1) which has a different carbohydrate structure, in immunodiffusion and hemagglutination inhibition tests. The presence of H-D antigen on MD lymphoma-derived cell lines MSB1 and HP1 was demonstrated using these antisera and purified antibodies by the indirect and/or direct membrane immunofluorescence technique and the complement-dependent antibody cytotoxicity test. However, weak or negative reactions were observed with the transplantable MD tumor-derived cell lines RP1 and BP1, and the avian lymphoid leukosis lymphoma-derived cell lines 1104B1 and 1104X5. These results suggest that so-called MATSA, recognized by chicken anti-MSB1 sera, consists of at least two different antigens: one is H-D antigen and the other has an unknown chemical nature. (Author abstract) (44 Refs)

TUMOR ASSOCIATED TRANSPLANTATION ANTIGENS

30. RESISTANCE OF THE METH A SARCOMA-ASSOCIATED REJECTION ANTIGEN TO INACTIVATION WITH GLUTARALDEHYDE.

Price MR, Gerlier D, Law LW
Cancer Res. Campaign Laboratories, Univ. Nottingham, Nottingham NG7 2RD, England
Br J Cancer; 44(4):584-587 1981

Immunogenicity of 3-methylcholanthrene-induced murine sarcoma (Meth A) subcellular fractions after treatment with glutaraldehyde (GLA) was examined. Treatment of Meth A plasma membranes or cytosol did not reduce their capacity to confer resistance to the tumor-cell challenge. Even cells fixed with 0.01% GLA, freeze-thawed 3x and sonicated, extracted further with 1% NP40, and re-sonicated were immunogenic, such that all treated mice survived the challenge of 10(4) viable Meth A cells. Meth A nuclei were immunogenic. Specificity of immunogenicity was tested by re-challenging surviving mice with 5 x 10(4) mKSA sarcoma cells; 90% of these mice died as a result of tumor growth. The present findings agree with the view that Meth A sarcoma-associated rejection antigen is a soluble protein which is expressed intracellularly. Interpretation of data in terms of antigen localization following subcellular fractionation of tumor homogenates should be cautious. (11 Refs)

31. RUNT DISEASE IN MICE AFTER PRETREATMENT OF THE MOTHER WITH TUMOR ANTIGENS.

Matusevich M, Piazzon I, Deroche A, Pasqualini CD
Istituto de Investigaciones Hematologicas, Academia Nacional de Medicina, Las Heras 3092, 1425 Buenos Aires, Argentina
Medicina (B Aires); 41(3):321-327 1981

Ability of a tumor of non-paternal origin to induce maternally acquired runt disease and the relation of fetal damage to mode of presentation of tumor antigen were examined. Protocols conditioning for tumor enhancement and those leading to tumor rejection were compared. Two experimental models were used: (1) female BALB mice immunized with AKR lymphoma L15 before mating with AKR males and (2) female Swiss mice immunized with Sarcoma 180 (S 180) before mating with Swiss males. The rejection protocol involved sc tumor challenge 1 wk before mating. Enhancement protocols in decreasing order of effect were (a) acetone-treated acellular tumor extract ip 4 days before mating (AE-Ac), (b) acellular tumor extract ip 4 days before mating (AE), and (c) tumor challenge by glass cylinder route (GC) 1 wk before mating. All litters were approx normal in size (6.6-11.6 offspring/mother). Runt disease leading to death before day 30 was directly proportional to degree of tumor enhancement. Highest death rates were observed in litters of mothers immunized with AE-Ac extracts of L15 (27/42; 64%) and of S 180 (29/53; 55%). Lowest rates were seen in offspring of mothers receiving sc tumor challenge of L15 (15/87; 17%) and S 180 (13/37;35%). Untreated BALB and Swiss litters exhibited significantly lower rates (9/134; 7% and 6/70; 8%, respectively). The GC route increased runt disease incidence; death occurred in 21/57 (37%) offspring of mothers inoculated with AKR splenocytes in GC, as compared with 1/33 (3%) from mothers receiving similar sc inoculation. Results of graft vs host assay performed at the time of mating in BALB mothers paralleled the incidence of runt disease. Findings indicate that tumor antigens can cause maternally induced runt disease even when unrelated to the paternal strain; the route of antigen presentation which favors immunological enhancement yields the highest incidence of runt disease. Mechanism for fetal damage and nature of the immunogen responsible for the maternally-induced runting are discussed. (18 Refs)

CLINICAL DIAGNOSTIC STUDIES

32. IN VIVO TUMOR LOCALIZATION USING TUMOR-SPECIFIC MONKEY XENOANTIBODY, ALLOANTIBODY, AND MURINE MONOCLONAL XENOANTIBODY.

Stuhlmiller GM, Sullivan DC, Vervaert CE, Croker BP, Harris CC, Siegler HF
Duke Univ. Medical Center, Box 3917, Durham, NC, 27710
Ann Surg; 194(5):592-601 1981

Specific in vivo localization of antibodies reactive with human melanoma cell membrane tumor associated antigens (TAA) has been attempted using congenitally athymic nude mice bearing sc human melanoma tumor xenografts as the experimental model. IgG fractions were prepared from each of several immune and control sera. Antimelanoma antibody sources included human alloantibody obtained from melanoma patients immunized against allogeneic melanoma cells, a monkey antiserum raised by immunization against a single human melanoma cell line, and a murine monoclonal antimelanoma antibody-secreting hybridoma cell line. Localization of these radiolabeled antibodies and of control IgG preparations to tumor tissue was determined by whole body scintigraphy and by differential tissue counting. Compared with the different control IgG preparations, each of the antimelanoma IgG preparations exhibited significant specific accumulation within the melanoma tissue. However, variation existed in the ability of each antimelanoma IgG to tumor prep aration to localize despite attempts to control model parameters such as tumor source, in vivo passage number and mass. This variation appears to reflect basic biologic differences between tumors in different animals and possibly differences in the antigen-binding capacities of each IgG preparation following radioiodination. This technique for tumor localization is very promising and has obvious potential for clinical application. (Author abstract) (16 Refs)

33. SEVERAL MARKER ANALYSES OF T-LYMPHOMA CELLS IN EIGHT JAPANESE ADULTS.

Nasu K, Tatsumi E, Takiuchi Y, Kita K, Nishikori M, Shirakawa S, Uchino H
First Div. Internal Medicine, Faculty Medicine, Kyoto Univ., Sakyo-ku Kyoto 606, Japan
Am J Clin Pathol; 76(5):670-678 1981

Lymphoma cells in eight adult Japanese patients with no evidence of overt leukemia throughout their clinical course were demonstrated to be of T-cell nature by combining studies of various immunologic cell surface markers and cytochemistry. The histologic diagnosis of these patients was diffuse histiocytic lymphoma in four patients, poorly differentiated lymphocytic lymphoma in two patients and mixed histiocytic and lymphocytic lymphoma in two patients, according to Rappaport's classification. In seven of the eight patients, the malignant appearance and the large number of E-rosetting cells readily led to the diagnosis of T cell lymphoma. Human Ia-like antigens were unexpectedly detected on the malignant T cells in seven of the eight patients. TdT activity was elevated in two of the four patients tested. Acid phosphatase activity was always observed in the neoplastic T-cells, and this activity was tartrate resistant. Focal activity of acid alpha-naphthyl acetate esterase was detected in the malignant cells with somewhat mature appearances, but large immature cells had no or weak dispersed activity. Except for E-rosetting ability, malignant T-cells showed such variable properties that multiple marker analyses seem to be necessary in the diagnosis and the prediction of prognosis of these disorders. Frequent occurrence of T-cell malignancy in Japan was also discussed. (Author abstract) (52 Refs)

34. IMMUNE MARKER ANALYSIS OF CSF CELLS IN THE DIAGNOSIS OF CNS LEUKEMIA IN CHILDHOOD ACUTE LEUKEMIA (MEETING ABSTRACT).

Thoene I, Woempner R, Matzke E, Kabisch H, Winkler K, Landbeck G
University of Hamburg 20, 2000 Hamburg, W. Germany
Exp Hematol; 9(Suppl9):83 1981

In a preliminary study cerebrospinal fluid (CSF) samples of children with acute leukemia were analyzed with antisera against the 'common' acute lymphocytic leukemia (ALL) antigen, Terminal Transferase enzyme protein, thymocyte antigens, surface immunoglobulin and with a phagocytosis test. All patients showed mild to massive pleocytosis. In 20 cases CSF cells were checked for the 'common' ALL antigen. In 10 cases with morphologically detected blasts different proportions of abnormal cells reacted with the anti-cALL-antiserum. Three of 10 CSF samples with lymphocytic pleocytosis contained a population of cALL + cells of lymphocytic appearance but the patients remained in remission. However, one suffered from a cALL + bone marrow relapse four mo later. In accordance with the morphological diagnosis 7 cases in clinical remission had no cALL + cells in the CSF. All CSF cells from one patient with a lymphocytosis of greater than 1000/ul reacted with an anti-thymocyte-antiserum but only 45% of these cells contained terminal deoxynucleotidyl transferase (TdT) whereas 82% of bone marrow cells showed strong TdT positivity at the time. All cells were strongly positive in the phagocytosis test. In bone marrow relapse half a yr later the same patient showed 30% phagocyting blasts which all reacted with the anti-immunoglobulin-antiserum. It is concluded by this study that immunemarker analysis of CFS cells may be an important aid for the diagnosis of CNS leukemia even in relapse or sometimes for the initial diagnosis if there is no other cell source. (no Refs)

35. T LYMPHOCYTE SUBSETS IN B CHRONIC LYMPHOCYTIC LEUKEMIAS AS DEFINED BY MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

Semenzato G, Foa R, Lauria F, Gobbi M, Gasparotto G
Universita di Padova, Padova, Italy, Pezzutto, A.
Exp Hematol; 9(Suppl9):167 1981

Most Chronic Lymphocytic Leukemias (CLL) are characterized by the monoclonal proliferation of B cells. In many CLL patients the absolute number of T lymphocytes is also increased; however the nature and function of these cells have not been completely defined. Several approaches have been tried to determine whether abnormalities of immunoregulatory T cell are associated with this increase. For this analysis we used monoclonal antibodies to the cell surface antigens of helper (OKT4) and suppressor (OKT8) T cell subsets and to a common T cell antigen (OKT3) defining all peripheral T cells. Twenty patients with CLL of B cell type were studied. T cells were separated from peripheral blood by rosetting with sheep RBC; repeated cycles of sedimentation on Ficoll-Hypaque gradients were done in order to obtain highly purified T cell populations. Analysis of this enriched population was performed with OKT series monoclonal antibodies by means of indirect immunoflurorescence with fluorescein-conjugated goat anti-mouse IgG. T cells from B-CLL patient showed an increase in T8 positive cells (44%) and a marked decrease in T4 cell subset (36%) with a reversed T4/T8 ratio. A correlation was also attempted with the T cell subsets defined by Fc receptors. Although no correlation between TM-TG lymphocytes and subsets defined by OKT4-OKT8 monoclonal antibodies was found, in both systems we observed an increase in suppressors and a loss of inducer cells. These results further suggest that immunoregulatory abnormalities exist in residual T cells from B-CLL. (no Refs)

36. MEMBRANE PHENOTYPING OF HUMAN LEUKEMIAS BY MURINE MONOCLONAL HYBRIDOMA ANTIBODIES: COMPARATIVE STUDIES BETWEEN 55 LEUKEMIA CELL LINES AND 88 FRESH LEUKEMIAS (MEETING ABSTRACT).

Tatsumi E, Sugimoto T, Sagawa K, Minato K, Srivastava SB, Han T, Ozer H, Preisler H, Freeman AI, Henderson ES, Minowada J
Roswell Park Memorial Institute, Buffalo, NY
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

A total of 55 proven human leukemia cell lines and 88 patients with 4 major types of leukemias were studied by multiple marker analysis. The 55 leukemia cell lines included those of 15 T-cell leukemia, 30 B-cell leukemia-lymphoma, 3 myeloid leukemia and 7 non-T, non-B cell leukemia-lymphoma origins. The fresh leukemia cells studied from 88 patients included 39 patients with acute lymphoblastic leukemia (ALL), 19 patients with acute myeloblastic leukemia (AML), 21 patients with chronic lymphocytic leukemia (CLL) and 9 patients with chronic myelocytic leukemia in blastic phase. In addition to the previously-employed conventional multiple marker analysis consisting of rosette assays and immunofluorescence assays, a total of 32 murine monoclonal hybridoma antibodies with respective specificity was used for further characterization of leukemia-lymphoma cells. It was found that no single markers defined by either conventional polyclonal antibody or monoclonal antibody were of leukemia specific. A considerable heterogeneity in the marker profile by the multiple marker assay was indeed observed in both leukemia-lymphoma cell lines and fresh leukemias. While the definitive markers, such as T-antigen, Ig and myeloid-cell antigen defined by the available polyclonal antibodies determined positively the leukemia cells in question into a definitive lineage in the hematopoiesis, other nondefinitive markers, such as Ia, common ALL antigen, TdT antigen and certain antigens defined by the monoclonal antibodies, permitted individual leukemia for further delineation as to degree of hematopoietic differentiation. On the other hand, some of the monoclonal antibodies did not reveal any apparent association with hematopoietic cell differentiation. (no Refs)

37. INCREASED FREQUENCY OF THE GROUP 5A ANTIGEN IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES.

Warren RP, Storb R, Nelson NJ, Sale GE, Thomas ED
Div. Oncology, Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
Tissue Antigens Histocompat Immunogenet; 18(2):85-91 1981

We have confirmed our previously described finding that the Group-5a antigen is associated with acute lymphoblastic leukemia. In addition we have found that the 5a antigen has an increased frequency in patients with chronic lymphocytic lymphoma but not in patients with acute myelogenous leukemia, acute myelomonocytic leukemia, Hodgkin's disease or histiocytic lymphoma. (Author abstract) (23 Refs)

38. BIOSYNTHESIZED PRODUCTS OF CULTURED NEUROGLIAL CELLS: I SELECTIVE RELEASE OF PROTEINS BY CELLS FROM HUMAN ASTROCYTOMAS.

McKeever PE, Quindlen E, Banks MA, Williams U, Kornblith PL, Laverson S, Greenwood MA, Smith B
Surgical Neurology Branch, Natl. Inst. Neurological and Communicative Disorders and Stroke, NIH, Building 10A, Room 3E68, Bethesda, MD, 20205
Neurology (NY); 31(11):1445-1452 1981

The proteins synthesized and released by human astrocytoma cells cultured with radiolabeled amino acids were analyzed by polyacrylamide gel electrophoresis in sodium dodecyl sulfate and by trichloroacetic acid precipitation. A select group of extracellular proteins was released from the astrocytomas. The most abundant extracellular proteins were at least 250,000 daltons. Five other major proteins (P 175, P 125, P 60, P 47, and P40) were 175,000, 125,000, 60,000, 47,000, and 40,000 daltons, respectively. The complement of proteins retained by the cells was considerably more complex than those released. Clinical efforts to enhance the immunologic response directed against human astrocytomas must distinguish between extracellular and retained antigens. The pattern of proteins released by gliomas might be diagnostically useful if present in cerebrospinal fluid or serum. (Author abstract) (48 Refs)

39. A NEW TECHNIQUE FOR DETECTING ANTIGENS A, B, AND H IN THE DIAGNOSIS OF BLADDER TUMORS.

Raymond G, Hammou H, Fella C, Toubol J, Pastorini P, Masseyef R
Service d'Urologie, Hopital Pasteur, rue de la Voie-Romaine, 06000 Nice, France
Ann Urol (Paris); 15(5):329-332 1981

A study of the significance of the presence of surface antigens A, B, and H in bladder tumors of 29 patients is presented. In tumors of eight of the patients, the antigens were found during a follow-up period of at least 6 yr. The antigens were never found when the cancer was advanced or infiltrating; in patients for whom antigens were not found in superficial tumors, the prognosis and course of the disease were poor. Of the eight patients in whom antigens were found, four were cured without recurrence and four had recurrent disease. A decrease in antigenicity always preceded by 6 mo to 1 yr the aggravation of the disease. It was suggested that the absence or presence of surface antigens in bladder tumors has a prognostic value and is helpful in determining the potential for infiltration or recurrence of the cancer. (19 Refs) (In FRE)

40. INTESTINAL M3 ANTIGEN, A MARKER FOR THE INTESTINAL-TYPE DIFFERENTIATION OF GASTRIC CARCINOMAS.

Bara J, Hamelin L, Martin E, Burtin P

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Int J Cancer; 28(6):711-719 1981

The mucus-associated intestinal M3 antigen, normally restricted to intestinal goblet cells, was found in 35 out of 100 gastric adenocarcinomas belonging to intestinal (19/64) as well as diffuse (16/36) types according to Lauren's classification, often accompanying the other mucus-associated gastric M1 and M2 antigens. This M3 antigen was predominant over the gastric M antigens in 25 of these 35 tumors; 18 of these belonged to the histological intestinal type. According to the WHO classification, the M3 antigen was found to predominante in all mucinous adenocarcinomas (7/7), was never present in the undifferentiated carcinomas (0/8), but was also found in some tubulo-papillar (16/57) and signet-ring cell (12/27) adenocarcinomas. This antigen could be used as a new criterion and incorporated into a point system containing morphological and tumor cell behavioral considerations; then it would appear to be a good marker for intestinal-type differentiation. Indeed, 22 of these 25 gastric adenocarcinomas which produced predominantly M3 antigen showed such an intestinal-like differentiation. The M antigenic pattern of gastric carcinoma suggested a duodenal rather than colonic-type differentiation. (Author abstract) (36 Refs)

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DETECTION/ CHARACTERIZATION/ ISOLATION

1. HUMAN T CELL LEUKEMIA ANTIGENS ON THE CELL MEMBRANES: PURIFICATION, MOLECULAR CHARACTERIZATION, AND PREPARATION OF SPECIFIC ANTISERA.

Seon BK, Negoro S, Minowada J, Yoshizaki K
Dept. Immunology Res., Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
J Immunol; 127(6):2580-2588 1981

Human T cell leukemia-associated (HTL) antigens were isolated from cell membranes of two T leukemia cell lines, MOLT-4 and JM, without using radiolabeling. We isolated milligram quantities of a human leukemia-associated cell membrane antigen preparation that contained a single immunodominant glycoprotein of 100,000 mol wt composed a single polypeptide chain. This 100,000 mol wt glycoprotein together with the 54,000 mol wt glycoprotein are the first reported human leukemia-associated cell membrane antigens that were identified as isolated proteins without the aid of radiolabel markers. (54 Refs)

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2. CLONING OF A FUNCTIONAL GENE RESPONSIBLE FOR THE EXPRESSION OF A CELL SURFACE ANTIGEN CORRELATED WITH HUMAN CHRONIC LYMPHOCYTIC LEUKEMIA.

Stanners CP, Lam T, Chamberlain JW, Stewart SS, Price GB

Dept. Medical Biophysics, Univ. Toronto, Ontario Cancer Inst., 500 Sherbourne St., Toronto, Ontario M4X 1K9, Canada

Cell; 27(1,part2):211-221 1981

A cell-cell hybrid of a Chinese hamster ovary (CHO) cell line and human peripheral blood lymphoblasts from a patient with B-cell chronic lymphocytic leukemia produces a surface antigen detectable by a monoclonal antibody. This surface antigen can be detected at significant levels on a fraction of chronic lymphocytic leukemia cells, but not on normal human lymphocytes from peripheral blood or bone marrow. Two different clones capable of transforming mouse cells to produce the surface antigen were isolated from a gene library of the hybrid cell by identification of small portions of the library containing functional genes, followed by detection of clones with human-specific reiterated sequences. Both clones also contain CHO-specific reiterated sequences and are therefore human-CHO recombinants. From the frequency of antigen-producing clones in the library, we estimate that they were present in the hybrid cell genome at a copy number of 100 to 1,000. (Author abstract) (32 Refs)

3. HIGH LEVELS OF 5'-NUCLEOTIDASE ACTIVITY IN BLASTIC CHRONIC MYELOGENOUS LEUKEMIA WITH COMMON ALL-ANTIGEN.

Gutensohn W, Thiel E

Arbeitsgruppe Biochemische Humangenetik, Institut fur Anthropologie und Humangenetik, Schillerstrasse 42, D 8000 Munich 2, W. Germany

Leuk Res; 5(6):505-510 1981

Levels of 5'nucleotidase (5'-N) on surfaces of leukemia cells were determined for 44 patients in lymphoid blast crisis (LY-BC) of chronic myelogenous leukemia (CML) with or without common acute lymphoblastic leukemia (cALL) antigen (cALLA) and for 52 patients with acute myeloblastic (AML) or acute lymphoblastic (ALL) leukemia. The 5'-N activities of mononuclear cell preparations from 50 healthy blood donors ranged from 1.2 to 14.5 nanomoles AMP hydrolyzed/hr/10(6) cells; this activity was mainly due to T and B lymphocytes. In 12 cases of cALL, blast cells derived from blood and bone marrow of the same patient were compared; no difference in immunological phenotype expression was noted, and the 5'-N activity was the same in both cell sources. Cells from the AML patients, diagnosed mainly on the basis of hematological criteria, were cALLA-negative. Diagnosis of the cALL patients was based on the absence of B or T markers and the expression of cALLA. The difference in 5'-N activities of AML and cALL cells and the difference in 5'-N activities of myeloid blast crisis (MY-BC) and LY-BC cells were both statistically significant . A wide overlap in 5'-N activities for AML and cALL limits the usefulness of the 5'-N determination. No overlap of 5'-N activity was observed, however, for the LY-BC and MY-BC cells. The LY-BC cells of CML characterized by cALLA had high 5'-N levels, while cALLA-negative blast crisis was correlated with a decrease in 5'-N activity. The results indicated that 5'-N affords an additional, easily-testable biochemical marker that may have diagnostic and prognostic value in blastic CML. (31 Refs)

4. BIOCHEMICAL AND IMMUNOLOGICAL CHARACTERIZATION OF CELLULAR DNA POLYMERASES ALPHA, BETA AND GAMMA, AND A REVERSE TRANSCRIPTASE FROM HUMAN MELANOMA TISSUE.

Chandra P, Balikcioglu S, Mildner B

Zentrum der Biologischen Chemie, Theodor-Stern-Kai 7, D-6 Frankfurt a. Main 70, W. Germany

Cell Mol Biol; 27(2/3):239-251 1981

The present study describes separation and purification of a reverse transcriptase and cellular DNA polymerases from human primary melanoma tissue. The specific requirements with respect to bivalent cations and template-primers for DNA polymerase alpha, DNA polymerase beta and DNA polymerase gamma, as well as for the reverse transcriptase, are reported. Sodium dodecylsulfate gel electrophoresis of the purified enzymes gave estimated values of mol wt of 160,000, 38,000, 100,000 and 68,000 daltons for DNA polymerase alpha, DNA polymerase beta, DNA polymerase gamma and reverse transcriptase respectively. Serological studies have shown that the reverse transcriptase of human melanoma tissue is not antigenically related to cellular DNA polymerase alpha, beta, or gamma, but is antigenically related to reverse transcriptases from baboon endogenous virus (BEV) and RD-114. This is the first human reverse transcriptase showing cross-reactivity to DNA polymerases from endogenous retroviruses. (Author abstract) (24 Refs)

5. HUMAN LYMPHOCYTE SURFACE ANTIGENS. PART 1. PRODUCTION AND CHARACTERIZATION OF HETEROANTISERA AGAINST CELL LINES DERIVED FROM T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA AND ADULT T-CELL LEUKEMIA.

Yoshimoto S

Second Dept. Internal Medicine, Okayama Univ. Medical Sch., Okayama, Japan

Nippon Ketsueki Gakkai Zasshi; 44(6):1153-1162 1981

Two heteroantisera were produced by immunizing NZW rabbits with cells of TALL-1 or MT-1. These antisera were rendered T-cell specific after absorption with human RBC acute myelogenous leukemia cells, surface Ig-positive chronic lymphocytic leukemia cells and several non-T lymphoblastoid cell lines. Absorbed antisera, anti-TALL-1 and anti-MT-1, were tested for reactivities with normal and malignant T-cells and cells of other hematological malignancies by indirect membrane immunofluorescence. Anti-TALL-1 and anti-MT-1 were uniformly reactive with normal thymocytes and peripheral blood T-lymphocytes, and their reactivities against these two populations of T-cells were almost completely abolished by absorption with normal thymocytes or peripheral blood lymphocytes (pbl). However, different reactivities were observed between these antisera. (1) Anti-TALL-1 was highly reactive with cells of T-ALL cell lines but only minimally with MT-1 and ATL cells. On the other hand, anti-MT-1 was highly reactive with MT-1 and ATL cells whereas its reactivities with cells of T-ALL cell lines were variable (10-67%). (2) Absorption of anti-TALL-1 with MT-1 cells eliminated reactivities with ATL cells but not with normal thymocytes and pbl. Similarly, absorption of anti-MT-1 with TALL-1 cells eliminated reactivities with T-ALL cell lines but not with normal thymocytes and pbl. There seems to be at least two distinct differentiation antigens in the normal T-cell series. One is recognized by anti-TALL-1 and the other by anti-MT-1. Antigens of T-ALL and ATL cells are distinct from those of normal T-cells. Antigens of ATL cells are homogeneous while those of T-ALL cells more heterogeneous and thus T-ALL may be further divided into subgroups. (44 Refs) (In JPN)

6. MYELOID DIFFERENTIATION ANTIGEN DEFINED BY A MONOCLONAL ANTIBODY.

Majdic O, Liszka K, Lutz D, Knapp W
(c/o Knapp), Inst. Immunology, Borschkegasse 8A, A-1090, Vienna, Austria
Blood; 58(6):1127-1133 1981

A monoclonal antibody of the IgM kappa type directed at a determinant on K-562 cells was produced and characterized. This hybridoma antibody, provisionally termed D5, defines a membrane-associated antigen that seems to be restricted, within the hemopoietic system, to the granulocytic cell lineage and possibly also to very immature erythroid and monocytic cells. Within the granulocytic cell lineage, D5 antibody reacts with all differentiation stages starting from the promyelocyte up to and including the mature granulocyte. Normal and malignant myeloblasts are only weakly positive or negative. Within the monocytic cell lineage, only fairly immature malignant cells as represented by cells from two patients with monoblastic leukemia and by two monoblastoid cell lines were found to be strongly D5 positive. Among the mature glass-adherent monocytic cells from normal peripheral blood, only very few cells react with D5 antibody. The fact that we have raised this antibody against cells (K-562) that are considered to represent very immature erythroid precursor cells would suggest that normal erythroid precursors should also be D5 positive. However, so far we are unable to detect such cells. Therefore, the proportion of D5-positive erythroid precursors resembling the K-562 cell type must either be very low in the bone marrow, or the D5 antigen is not present on normal erythroid precursor cells and only aberrantly expressed on K-562 cells. Mature erythrocytes are also D5 negative. There was no evidence that lymphoid precursors react with D5 antibody, in that all normal and malignant lymphoid cells tested so far were D5 negative. Further, platelets showed no reactivity with D5 antibody. (Author abstract) (40 Refs)

7. A MONOCLONAL ANTIBODY WHICH IDENTIFIES A SUBPOPULATION OF HUMAN B LYMPHOCYTES AND MONOCYTES (MEETING ABSTRACT).

Munchus MS, Levitt D
University of Illinois Medical Center, Chicago, IL, 60612
Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

Hybridoma antibodies were produced against the 'pre-B' lymphoblastoid cell line, Nalm-6. A subclone of one of these hybridoma antibodies (1-96) identifies a determinant on the surface and in the cytoplasm of Nalm-6 and 6 of 11 human lymphoblastoid cell lines. The intensity of reaction of 1-96 was greatest in cell lines with large numbers of cytoplasmic vesicles. I-96 identifies a different determinant than another monoclonal antibody specific for a common acute lymphoblastic leukemia antigen (J5). Furthermore, MABI-96 specifically reacts with a surface determinant on a subpopulation of slg+ and clg+ cells from peripheral blood, spleen, and tonsil, and with a subpopulation of G-10 adherent, OKMI+ cells. The I-96 antigen does not associate preferentially with any class of immunoglobulin and I-96 does not react with T cells. When PBMC are stimulated with the polyclonal B cell activators pokeweed mitogen and Staphylococcus aureus (Cowans I) the number of MABI-96+/slg+ cells decreases sharply. In unstimulated cultures the percentage of such cells markedly increases by day 4, followed by a gradual decrease toward the end of the culture period. It appears that this antibody defines a functional subpopulation of human B lymphocytes and monocytes. (no Refs)

8. CELL SURFACE ANTIGENS OF X-RAY INDUCED LYMPHOMA: DETECTION AND CHARACTERIZATION USING MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

Allison JP
The University of Texas System Cancer Center, Science Park, Smithville, TX, 78957
Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.

The cell surface antigenic mosaic of an x-ray induced lymphoma of C57BL/6 mice has been examined using conventional and monoclonal antibodies. The tumor cells display four glycoproteins related to murine leukemia virus (MuLV) - two env and two gag gene products. Immunization of syngeneic mice with tumor cells elicited formation of antibodies to only one of the two MuLV env proteins. Analysis with monoclonal antibodies revealed that this antigen was antigenically related to ecotropic MuLV. One hybridoma clone, designated 124-40, produced by fusion of spleen cells from C6XL-immunized BALB/c mice with P3 myeloma cells, secreted monoclonal antibodies (McAb) which reacted with tumor cells, but not with normal lymphoid cells. The tumor associated antigen reative with McAb 124-40 was found to be a glycoprotein with subunit mol wt of approx 40 Kd, and was structurally and immunologically distinct from MuLV antigens on the tumor cells. The antigen was not found on adult spleen, thymus, bone marrow, or lymph node cells, nor on fetal thymus or spleen. Two additional x-ray lymphoma lines, as well as three spontaneous leukemias of AKR mice, were also unreactive with McAb 124-40. Administration of the McAB 124-40 to tumor-bearing mice resulted in a slight increase in survival time. The therapeutic effect was greatly enhanced by administration of McAb conjugated to the cellular toxin pokeweed antiviral protein. (no Refs)

IMMUNOLOGICAL STUDIES

9. HUMAN CANCERS TRANSPLANTED IN NUDE MICE RETAIN THE EXPRESSION OF THEIR ORGAN-SPECIFIC NEOANTIGENS.

Thomson DM, Neville AM, Phelan K, Schwartz Scanzano R, Vandevoorde JP
Montreal General Hosp., Montreal General Hosp. Res. Inst., 1650 Cedar Ave., Montreal, Quebec H3G 1A4, Canada
Eur J Cancer Clin Oncol; 17(11):1191-1197 1981

Human cancers transplanted to nude mice seem to retain most features of the original tumor. To determine if organ-specific neoantigens were still expressed after transplantation, four different human cancers, supplied and coded by independent investigators, were assayed in the tube LAI assay. The LAI phenomenon measures the change in adherence properties of leukocytes that have bound an antigen to which they are sensitized immunologically. Four of four transplanted human cancers - pancreas, lung, breast, and colon - stimulated an LAI+ response with leukocytes from patients with cancers of the same organ. The antitumor response was not a vigorous against a pool of transplanted tumor extracts as against those prepared from liver metastases. Nonetheless, the results add to the mounting evidence that human cancers express neoantigens to which most humans bearing cancers respond immunologically. (Author abstract) (31 Refs)

10. SOMATIC CELL HYBRID ANALYSES OF HEMATOPOIETIC DIFFERENTIATION.

Koeffler HP, Sparkes RS, Billing R, Klein G

Dept. Medicine, Div. Hematology-Oncology, Univ. California Los Angeles Center Health Sciences, Los Angeles, CA, 90024

Blood; 58(6):1159-1163 1981

A differentiated cell expresses an entire set of specialized features. Somatic cell hybridization provides a method to examine control of gene regulation. We studied the expression of tissue-specific features in hybrids between human promyelocytes (HL-60) and human Burkitt's lymphoma cells (P3HR-1). Two hybrid lines, HP-1 and HP-2, and 18 hybrid clones were established and confirmed by karyotype, isozyme, and surface antigen analyses. The hybrids extinguished the 10 myeloid (HL-60) features that we examined including myeloid morphology, histochemistry, and functions that included response to colony-stimulating factor and ability to differentiate to granulocytes or macrophages. In contrast, the hybrids synthesized immunoglobulin and expressed Epstein-Barr nuclear, early, and viral capsid antigens similar to the P3HR-1 lymphoid parental line. Results are contrasted to the findings when P3HR-1 lymphocytes are fused to human erythroid-myeloid cells (K562). Taken together, our results suggest that phenotypic differences between human myeloid and lymphoid cells in the hematopoietic lineage involve mutually exclusive programs and may possibly be mediated by the activity of diffusible, transacting molecules. (Author abstract) (28 Refs)

11. THE IMMUNOTHERAPEUTIC EFFECT OF A POLYANTIGENIC VACCINE IN ANIMAL TUMOR MODELS.

Colon JI, Marchand AM, Roman Franco AA, Santiago Delpin EA

Puerto Rico Cancer Center, Puerto Rico

Bol Asoc Med P R; 73(4):162-167 1981

A polyantigenic vaccine (PAV) was tested against mouse Ehrlich ascites tumor (EAT), adenocarcinoma (AC), and chondrosarcoma (CS) in BALB/c and C3H/HeJ mice. Tumor inoculations consisted of 10(5) cells injected sc. PAV consisted of influenza virus and bacterial vaccines suspended in peanut oil and Arlacel A. Doses of 0.1 ml PAV were given weekly, beginning 1 wk after tumor inoculation. Tumors developed in 37.5% of PAV-treated AC-bearing mice compared with 87.5% of untreated controls. Mortality rate was 71% among controls and 0% among PAV-treated mice. PAV-treated EAT-bearing mice showed a 44% mortality rate compared with 89% for untreated controls. EAT growth resumed if PAV treatment was stopped. BCG treatment protected 10% of CS-bearing mice, while PAV protected 50%. Together PAV and BCG protected 58% of CS-bearing mice. All untreated controls died. The viral component of PAV was more active than the bacterial component, but not as effective as complete PAV. Results indicate the effectiveness of PAV against some experimental tumors. (5 Refs)

12. CHARACTERISTICS OF AN ANTIGEN-SPECIFIC HELPER FACTOR THAT ENHANCES THE IN VITRO GENERATION OF CYTOTOXIC CELLS DIRECTED AGAINST A SYNGENEIC TUMOR.

Kilburn DG, Talbot FO, Levy JG

Dept. Microbiology, Univ. British Columbia, Vancouver, B. C., V6T 1W5, Canada

J Immunol; 127(6):2465-2469 1981

An antigen-specific helper factor (Hf) that enhances the in vitro generation of tumor-specific cytotoxic T cells (CL) has been isolated from the spleens of DBA/2 mice bearing the syngeneic mastocytoma, P815. This factor enhances the CL response to P815 but not to L1210 (a syngeneic T cell leukemia in DBA/2 mice), B10 minor antigens, or DBA/2 alloantigens. The factor binds specifically to P815 membrane immunoadsorbent columns and can be eluted with 2 M NaCl. P815 Hf did not resemble the lymphokine IL 2 because it did not enhance the proliferative or CL response of thymocytes nor would it support the growth of an IL 2-requiring line of T cells. This factor acted optimally if added late in the culture period in contrast to IL 2, which was more effective if added early. In limiting dilution experiments P815 Hf enhanced the level of CL activity generated but not the number of precursors triggered. IL 2 markedly amplified both of these parameters. (Author abstract) (27 Refs)

13. MACROPHAGE ACCUMULATION IN TRANSPLANTED TUMORS IS NOT DEPENDENT ON HOST IMMUNE RESPONSIVENESS OR PRESENCE OF TUMOR-ASSOCIATED REJECTION ANTIGENS.

Evans R, Eidlen DM
Jackson Lab., Bar Harbor, ME, 04609
J Reticuloendothel Soc; 30(5):425-437 1981

The macrophage content of three chemically-induced C57BL/6J sarcomas growing in normal or immunosuppressed mice was assessed to determine whether host immune responsiveness or the presence of tumor-associated rejection Ags was important during monocyte infiltration or macrophage accumulation. Mice were immunosuppressed using various doses of whole body irradiation. Nude mice were also used. The data indicated that there was no relationship between the level of macrophages in a tumor and the ability of the host to mount an immune response or of the tumor to induce one. Moreover, it was apparent that the level of macrophages in a tumor was partly dependent on a critical number of circulating monocytes but not necessarily dependent on a normal blood monocyte count. The data are discussed in terms of possible mechanisms whereby monocytes infiltrate and accumulate in the tumor mass, where they presumably mature into the typical, phagocytic, non-specific, esterase-positive macrophage. (Author abstract) (16 Refs)

14. ANTIGENS DISPLAYED ON MURINE B LYMPHOCYTE PRECURSORS.

Kincade PW, Lee G, Watanabe T, Sun L, Scheid MP
Sloan-Kettering Inst. Caner Res., 145 Boston Post Road, Rye, NY, 10580
J Immunol; 127(6):2262-2268 1981

The surface antigen phenotype of the immediate precursors of clonable B Lymphocytes was investigated with conventional alloantisera and monoclonal antibodies directed to B lineage antigens. Ia was demonstrable on B cells, but not their immediate precursors in adult marrow. Adult, but not fetal, B cell precursors were susceptible to lysis with anti-Lyb-2 or Anti-Qa. A panel of monoclonal rat antibodies was prepared and placed into categories on the basis of recognition patterns obtained with established cell lines. Of two groups that are described here, in one (typified by antibodies from clone 14.8) we detect an antigen that is preferentially expressed on B cells and their precursors, a proportion of antibody-secreting cells, and a subpopulation of peripheral T lymphocytes. Cells that did not display demonstrable amounts of antigen include brain, granulocytes, macrophages, mastocytoma cells, and erythroleukemia cells. A second category of antibodies revealed an antigen that was more widely distributed on hemopoietic cells. Cells capable of quickly maturing into functional, colony-forming B lymphocytes in culture or after transfer to irradiated recipients specifically adhered to 14.8 antibody-coated, polystyrene petri dishes in the cold. Reductions in numbers of stem cells (CFU-s) and myeloid progenitors (CFU-c) by this treatment were minimal. Of particular importance was the fact that these antibodies recognized cells in embryonic liver as well as in adults that were destined to become B lymphocytes. These observations provide new perspective on B lineage precursor heterogeneity and suggest ways of localizing and dissecting some of the earliest events that are critical to development of the humoral immune system. (Author abstract) (51 Refs)

15. ACCESSORY CELLS IN THE IN VITRO GENERATION OF TYPE C VIRUS-SPECIFIC T KILLER LYMPHOCYTES: II. DEMONSTRATION OF A T HELPER CELL IN THE SPLEEN OF IN VIVO PRIMED MICE.

Gomard E, Wybier-Franqui J, Simmler MC, McKenzie IF, Levy JP
Laboratoire Immunologie et Virologie des Tumeurs, INSERM U 152, ERA 781, Hopital Cochin 27, rue du Faubourg Saint Jacques, 75645 Paris Cedex 14, France
J Immunol; 127(6):2291-2295 1981

The existence of a helper T cell cooperating with cytolytic T lymphocytes (CTL) in cell-mediated anti-tumor responses specific for the virus-induced FMR antigens can be demonstrated by using unprimed thymocytes as CTL precursors and in vivo primed irradiated spleen cells as helper. The helper T cells express Thy-1.2 and Lyt-1.2 antigens at their surface, but not Lyt-2.2. The helper function required the presence of macrophages to be detected, is antigen specific, and appears unusually radiosensitive compared with previously described helper T cell function. (Author abstract) (27 Refs)

VIRUS ASSOCIATED ANTIGENS

16. TYPE C VIRUS PARTICLES IN A CORD T-CELL LINE DERIVED BY CO-CULTIVATING NORMAL CORD LEUKOCYTES AND HUMAN LEUKAEMIC T CELLS.

Miyoshi I, Kubonishi I, Yoshimoto S, Akagi T, Ohtsuki Y, Shiraishi Y, Nagata K, Hinuma Y
Dept. Medicine, Kochi Medical Sch., Kochi 781-51, Japan
Nature; 294(5843):770-771 1981

Cocultivation of adult T-cell leukemia (ATL) cells with cord WBC from a male infant was used to establish a T-cell line that expresses ATL-associated antigens (ATLAs) and contains numerous C-type virus particles. The ATLAs were detected by indirect immunofluorescence using ATL patients' sera and fluorescein isothiocyanate-conjugated goat antihuman IgG. Thin-section electron microscopy revealed the virus particles, which are predominantly mature and consist of an electron-dense nucleoid and an outer membrane. (8 Refs)

17. THE 2.2 KB E1B MRNA OF HUMAN AD12 AND AD5 CODES FOR TWO TUMOR ANTIGENS STARTING AT DIFFERENT AUG TRIPLETS.

Bos JL, Polder LJ, Bernards R, Schrier PI, Van den Elsen PJ, Van der Eb AJ, Van Ormondt H

Dept. Medical Biochemistry, Sylvius Lab., Univ. Leiden, Wassenaarseweg 72, 2333 AL Leiden, The Netherlands

Cell; 27(1,part2):121-131 1981

By nucleotide sequence analysis and S1 nuclease mapping we have determined the structural organization of early region E1b of Ad12. We have also revised the nucleotide sequence of the E1b region of Ad5. Both regions have an identical structural organization and show considerable homology at the nucleotide level. The major tumor antigens (Ad12, 19 and 54 kilodaltons [kd]); Ad5, 21 and 55 kd are encoded in two overlapping reading frames. A single mRNA of 2.2 kilobases codes for both these proteins, depending on which AUG triplet serves as the start codon: the 19-21 kd protein initiates at the 5'-proximal AUG; the 54-55 kd protein initiates at the second AUG in another reading frame. Peptide mapping shows that the small and large tumor antigens do not share common tryptic peptides, in accordance with the nucleic acid sequence data. In addition, the 19-21 kd protein can also be synthesized from a one kilobase mRNA. Finally, the gene for the Ad12 analog of protein IX is characterized. (Author abstract) (48 Refs)

18. THE IMMUNOREGULATORY CHARACTERISTICS OF THE LACTIC DEHYDROGENASE VIRUS (LDV), A COMMON CONTAMINANT OF TUMORS.

Isakov N, Segal S, Feldman M

Dept. Cell Biology, Weizmann Inst. Science, Rehovot, Israel

Cell Mol Biol; 27(2/3):83-96 1981

A tumor-enhancing and antibody increasing spleen cell-associated factor originating in Lewis lung carcinoma (3LL)-bearing C57BL/6 mice was identified as the lactic dehydrogenase virus (LDV). A potent immunoregulating factor was obtained only following the inoculation of LDV-infected but not LDV-free tumor cells. The observed augmentation of humoral responses by an acute infection with LDV was found to be fully correlated with the ability of the virus to replicate and establish a persisting infection in the host. LDV caused an augmented humoral response in all mouse strains tested (causing a life-long viremia), but failed to influence the humoral response in rats, which are an LDV-resistant species. We found that although an infection with LDV causes a polyclonal B-cell activation it does not affect all of the different B-cell clones and in the presence of a specific antigenic stimulus it preferentially triggers the IgG2 subclass of antibody-secreting B cells. An acute LDV infection causes a substantial suppression of cell-mediated immunity functions and a delayed thyroid allograft rejection was demonstrated in infected mice. Since mononuclear phagocytes, which are the target cells of LDV, play an important role in cellular immune responses, we tested the immunogenic antigen-presenting capacity of LDV-infected macrophages, using a system in which in vitro reactivation of memory T cells is dependent upon effective specific antigen presentation by macrophages. We found that the antigen presentation capacity of macrophages from acute LDV-infected mice is impaired. These results may contribute to a better understanding of the ways in which mammalian RNA viruses may act as immunomodulators. (Author abstract) (42 Refs)

19. NEW ANTIGEN INDUCED BY HERPES SIMPLEX VIRUS IN HUMAN TUMORS.

Posevaia TA, Kosiakova NP, Barinskii IF, Kosiakov PN, Pavliuchenkova RP
D. I. Ivanovskii Inst. Virology, Moscow, USSR
Vopr Virusol; (5):597-601 1981

Infection of biopsy specimens of various human tumors with herpes simplex virus was found to induce a new antigen not only in neoplasms of the uterus, cervix, and ovary but also in those of the kidney and bladder. The antigens induced in the cervical carcinoma had the highest complement-fixation activity. (13 Refs) (In RUS)

20. THE HEPATITIS-B VIRUS AND HEPATOCELLULAR CARCINOMA.

Kew MC
Dept. Medicine, Witwatersrand Univ. Medical Sch., Johannesburg, South Africa
Semin Liver Dis; 1(1):59-67 1981

The association between hepatocellular carcinoma (HCC) and chronic hepatitis-B virus (HBV) is discussed, and various explanations for its etiology are considered. The world-wide geographic distributions of the HBV carrier state and HCC are remarkably similar, with some exceptions. Countries in sub-Saharan Africa and the Far East, eg, with HBV surface antigen carrier rates of 6-14% also have the highest rates of HCC. However, in Greenland, where 7-25% of the population has chronic HBV surface antigen, HCC is nevertheless rare. This discrepancy could be explained by the absence of a cocarcinogen in the Greenland environment. The most persuasive evidence that an association exists between HCC and HBV is the frequency with which markers of the virus are present in the serum and tissues of patients with this tumor. Alternative explanations to a cause and effect relationship between HBV infection and HCC are discussed. However, no such considered explanations account for the association as well as the postulate that HBV plays a causal role in HCC. (84 Refs)

21. INCORPORATION OF INFLUENZA VIRUS ANTIGENS IN AVIAN SARCOMA VIRUS ENVELOPE.

Migunova BV, Kuznetsov OK
Res. Inst. of Vaccines and Sera, USSR Ministry Health, Leningrad, USSR
Vopr Onkol; 27(10):63-67 1981

The mixture of influenza virus and pseudotype of Rous sarcoma virus RSV (PAB-A) grown in chick embryos or cell culture of chick fibroblasts produces a progeny which can be partially neutralized by a heterologous immune serum. The fraction of viral particles, the transformation activity of which is susceptible to suppression by both homologous anti-RSV (PAB-A) and heterologous serum, immune to influenza virus, amounts to approximately 20%. After passage, these particles lose this property which suggests a non-genetic character of the phenomenon. Hence, dual infection results in phenotypic mixing and formation of particles with nucleoprotein of RSV (PAS-A) which contain antigens of avian sarcoma and influenza viruses in their envelopes. (Author abstract) (8 Refs) (In RUS)

TUMOR ASSOCIATED TRANSPLANTATION ANTIGENS

22. GENERATION OF TUMOR-ENHANCING CELLS (TEC) AND TUMOR-NEUTRALIZING CELLS (TNC) BY TUMOR ANTIGEN.

Yamagishi H, Kodama M, Hashimoto I
Second Dept. Surgery, Kyoto Prefectural Univ. Medicine, Kamigyo-ku, Kyoto 602, Japan
Igaku No Ayumi; 117(3):128-130 1981

Sarcoma cells (MCA-F, -D, -C) induced by methylcholanthrene in 8-to 10-wk-old C3H/He mice were serially cultured in vivo. The crude antigen was extracted from these cells with 3 M KCL, and the tumor-facilitating antigen (TFA) and tumor protective antigen (TPA) were fractionated by preparative isoelectric focusing. The crude extract, TFA or TPA was injected sc into normal C3H/He mice and the spleen extirpated at various times later. The spleen cells and the tumor cells (MCA-F) were combined at a ratio of 1,000:1, and injected sc into the abdomen of 10 syngeneic C3H mice, then the diameter of the tumor was measured periodically. The same number of age-matched normal spleen cells and MCA-F were injected into the same number of mice as the controls. The spleen cells obtained 6 days after the crude antigen was inoculated had 118% (p less than 0.001) of the tumor-facilitating activity of the normal spleen cells, but those obtained on Days 9 and 12 had respectively 65% (p less than 0.01) and 43% (p less than 0.02) tumor-neutralizing activity. There was no significant difference between the activity of the spleen cells obtained 15 days after inoculation of the crude antigen and of normal spleen cells. When the spleen cells obtained 6 days after 14 ug of TFA was injected sc into the right abdomen were injected into normal mice together with tumor cells, the av diameter of the tumors produced 24 days after injection was 13.3 +-1.3 mm while it was 7.2 +-1.0 mm in the controls. On the other hand, the av tumor diameter was 3.6 +-0.6 mm when the spleen cells of the mice pretreated with TPA were injected together with the tumor cells. (2 Refs) (In JPN)

23. STUDIES OF TUMOR-SPECIFIC CELLULAR IMMUNE RESPONSES WITH SOLUBLE TUMOR ANTIGEN IN MICE. I. IMMUNOGENICITY OF HYPOTONIC SALINE EXTRACTS OF TUMOR CELLS.

Shibusawa M
Dept. Surgery, Showa Univ., Sch. Medicine, Shinagawa-ku, Tokyo 142, Japan
Nippon Geka Gakkai Zasshi; 82(6):566-574 1981

There are several assay methods to demonstrate cell-mediated immunity to the tumor of cancer patients. In these assays, usually whole tumor cells have been used as targets or immunogens for tumor sensitization. Suitable cell suspensions or cultures are rather difficult to prepare from the solid tumors. In order to prepare experimentally stable antigenic extracts easily, a soluble tumor antigen was prepared from mouse ascites hepatoma cells by a hypotonic saline extraction method. Immunogenicity of the hypotonic saline extracts was estimated by footpad assay for delayed cutaneous hypersensitivity and by lymphocyte blastogenesis to the tumor antigen (MLTR). Transplantability of the hepatoma cells was also tested in mice immunized with the soluble extract and BCG. In the footpad assay the immunized mice showed a higher response than the nonimmunized mice. In micro-MLTR studies, the optimum concentration of hypotonic saline extracts was 1.0 ug/ml and the max lymphocyte blastogenesis was observed on the 4th culture day. There was a significant relationship between the reaction in the footpad assay and the degree of lymphocyte blastogenesis. In the immunized mice, tumor-transplantation resistance and survival rate of the mice with growing tumors were higher than those in the nonimmunized mice. These results indicate that hypotonic saline extracts of tumor cells possess immunogenicity that could induce transplantation immunity when injected along with BCG. (43 Refs) (In JPN)

24. STUDIES OF TUMOR-SPECIFIC CELLULAR IMMUNE RESPONSES WITH SOLUBLE TUMOR ANTIGEN. II. KINETICS OF THE CELLULAR IMMUNE RESPONSES IN MICE WITH GROWING TUMORS.

Shibusawa M
Dept. Surgery, Showa Univ., Sch. Medicine, Shinagawa-ku, Tokyo 142, Japan
Nippon Geka Gakkai Zasshi; 82(7):693-701 1981

Measurement of cell-mediated immunity, specific and nonspecific, is important in estimating the prognosis and clinical state of cancer patients. In order to see what kinds of assays for cell-mediated immunity reflect the immunological state of cancer patients, kinetics of the cellular immune responses in C3H/He mice with growing MH134 tumors was carried out by the footpad assay, lymphocyte blastogenic response to a soluble tumor antigen (MLTR), leukocyte migration inhibition test (LMIT) using a soluble tumor antigen and lymphocyte blastogenic response to phytohemagglutinin (PHA) and concanavalin A (Con A). Soluble tumor antigens were prepared from MH134 cells by the hypotonic saline extraction method. These assays were carried out 0, 6, 8, 10, 13, 16 and 21 days after sc transplantation of MH134 cells. Footpad, MLTR and LMIT responses reached their max 10 days after tumor transplantation, and then decreased along with progressive tumor growth. The lymphocyte-blastogenic response to PHA reached a peak on day 6, Con A on day 8, and then both declined. A correlation between tumor diameter and PHA response was observed. An interesting significant relationship between the in vivo footpad reaction and the in vitro lymphocyte blastogenic responses to the tumor antigen and Con A was demonstrated. These results suggest that the measurement of immunological status with the use of a soluble tumor antigen might be useful for the study of specific immune responses in cancer patients. (17 Refs) (In JPN)

CLINICAL DIAGNOSTIC STUDIES

25. 10. POSSIBLE MECHANISMS OF IMMUNOTHERAPY ACTION IN ACUTE NONLYMPHATIC LEUKEMIA: MACROPHAGE PRODUCTION OF COLONY-STIMULATING ACTIVITY.

Reizenstein P, Andersson B, Beran M
Div. Hematology, Dept. Medicine, Karolinska Hosp., S-104 01 Stockholm, Sweden
Recent Results Cancer Res; 80:64-69 1982

Earlier studies show that immunotherapy (IT) improves prognosis in acute nonlymphatic leukemia (ANLL), and that ANLL cells probably have tumor-associated antigens, for autologous lymphocytes can react to them. Also, IT seems to immunize against allogeneic ANLL cells, but there is no cross-immunity to autologous ones. Moreover, patients immunized against their ANLL cells have no better prognosis than patients not having lymphocytes reacting to their ANLL cells. It has also been suggested that IT causes nonspecific immunostimulation, but IT patients' lymphocytes actually react less than those of patients not given IT. The current hypothesis is macrophage activation: Lymphocyte suppression in IT could be explained by suppressor macrophages. Colony-stimulating activity, produced by bone marrow macrophages, decreases during remission in patients not given IT, but not in IT patients. Numerically, blood cells from patients given IT form more colonies than those from patients not given IT. Three of eight patients given IT had more colonies than the upper normal limit. (Author abstract) (16 Refs)

26. TUMOR-ASSOCIATED CELL-MEDIATED IMMUNE RESPONSE OF GASTRIC CANCER PATIENTS: WITH PARTICULAR EMPHASIS ON CORRELATION WITH TUMOR BURDEN AND EFFECTS OF SURGICAL TUMOR REMOVAL.

Miyazaki M, Fujimoto S, Okui K
First Dept. Surgery, Sch. Medicine, Chiba Univ., Chiba, Japan
Nippon Gan Chiryo Gakkai Shi; 16(4):673-680 1981

Lymphoproliferative (LP) responses by allogeneic tumor extracts were compared with autologous responses to confirm the existence of common tumor-associated antigens (TAA) in gastric cancer (GC). The relationship between tumor burden and tumor-specific cellular immune response in GC was evaluated. The effect of surgical tumor removal upon tumor-specific cellular immune response was studied. Allogeneic TAA-induced LP responses of 38 GC patients were significantly superior (p less than 0.10) to those of normal subjects. Both allogeneic and autologous responses of resectable GC patients were remarkably superior (p less than 0.05) to those of normal persons, but no differences were found differences in av cancer specific stimulation index and ratio of autologous to allogeneic positive responses. Five of six GC patients with a positive response to autologous TAA had similarly positive responses to allogeneic TAA. Five of eight GC patients with a positive response to allogeneic TAA responded similarly to autologous TAA. The LP responses of the GC patients to allogeneic TAA were tested preoperatively and evaluated according to the clinical stage determined from the operative findings. The mean LP responses for stages I-IV were 1.14 +-0.25, 1.75 +-0.64, 1.92 +-0.87, and 0.93 +-0.21, respectively. Responses of all GC patients, including those with positive preoperative LP, decreased to within normal range 1 wk after resection and were virtually nil 1 mo after surgery. (22 Refs)

27. CLUSTERING OF HEPATITIS B VIRUS INFECTION AND HEPATOCELLULAR CARCINOMA IN A FAMILY.

Gilmore IT, Harrison JM, Parkins RA
Royal Liverpool Hosp., Liverpool L7 8XP, England
J R Soc Med; 74(11):843-845 1981

Family clustering of primary hepatocellular carcinoma (HCC) is well recognized, although rare. One possible reason for such clustering has become apparent since the advent of tests to detect circulating markers of hepatitis B virus infection, and this has been the common etiological factor in three families studied. We report the results of screening a Chinese family following the death of one member who had been found to have HCC associated with hepatitis B surface antigenemia. Four of seven siblings were traced: one had died of HCC 5 yr earlier, and evidence of past or present hepatitis B infection was found in the remaining three, one of whom was also found to have HCC. (Author abstract) (24 Refs)

28. LOCAL BCG-IMMUNOTHERAPY IN BLADDER CANCER PATIENTS: IMMUNOLOGICAL FOLLOW-UP STUDIES.

Seyfarth M, Hudemann B, Nizze H, Riedel H, Werner H
Dept. Immunology, Wilhelm Pieck Univ. Rostock, Leninallee 70, 2500 Rostock, E. Germany
Arch Geschwulstforsch; 52(1):63-66 1982

Local BCG therapy by intralesional injection produced some response in bladder tumors in 10/10 patients treated. Complete regression occurred in five patients. Immunological follow-up demonstrated increased leukocyte reactivity to tumor antigen in vitro (in electrophoretic mobility tests) in six patients and in vivo (in skin reactivity tests) in four patients. (9 Refs)

29. HUMAN PAPILLOMAVIRUS (HPV) IN CONDYLOMATOUS LESIONS OF CERVIX: A COMPARATIVE ULTRASTRUCTURAL AND IMMUNOHISTOCHEMICAL STUDY.

Ferenczy A, Braun L, Shah KV
Dept. Pathology, Jewish General Hosp., 3755 Chemin de la Cote Ste. Catherine, Montreal, Quebec H3T 1E2, Canada
Am J Surg Pathol; 5(7):661-670 1981

Cervical condylomata classified histologically as flat, papillary, or endophytic were obtained from 97 patients (16-35 yr old). Transmission electron microscopy (TEM) was used to detect the presence of human papillomavirus (HPV) particles; the immunoperoxidase technique (IPT) was used to detect viral antigen. HPV particles were found in 24/97 specimens by TEM. Viral particles were demonstrated in 21/68 flat and 3/26 papillary condylomata. Viral antigen was found in 47/97 specimens by IPT. All specimens positive by TEM were also positive by IPT, confirming the specificity of the immunological staining. The viral antigen was detected in 38/68 specimens of flat condylomata, in 9/26 papillary condylomata, and in 0/3 endophytic condylomata. Prevalence of HPV correlated with the extent of koilocytosis rather than with histiotype. IPT is of value for further characterizing cervical condylomata and the relationship between HPV infection and cervical intraepithelial neoplasia. (23 Refs)

30. ABNORMAL LYMPHOCYTES IN X-LINKED LYMPHOPROLIFERATIVE SYNDROME.

Seeley J, Sakamoto K, Ip SH, Hansen PW, Purtilo DT
Dept. Pathology, Univ. Massachusetts Medical Sch., Worcester, MA
J Immunol; 127(6):2618-2620 1981

Helper and suppressor T cells (labeled by OKT4 and OKT8 antisera, respectively,) were studied in males with X-linked proliferative syndrome (XLP), and in their mothers (carriers), asymptomatic brothers, maternally related male cousins (males at risk), and sisters (females at risk). Carrier mothers and both females and males at risk had normal mean percentages of OKT4 and OKT8 cells. However, XLP patients showed significantly lower OKT4 and higher OKT8 percentages compared with healthy controls; abnormally low OKT4:OKT8 ratios were expressed by 6/10 patients with hypogammaglobulinemia and/or lymphoma. Abnormally high OKT4:OKT8 ratios were found in several of 13 males at risk. Among the subjects at risk, OKT4:OKT8 ratios tended to be highest in those who had antibodies to Epstein-Barr virus (EBV) viral capsid antigen but not to EBV nuclear antigen. The ratios may useful in evaluating males at risk for XLP even before they become EBV-seropositive. (24 Refs)

31. IMMUNO-ELECTRON MICROSCOPY OF 'T' CELLS IN LARGE PLAQUE PARAPSORIASIS.

McMillan EM, Wasik R, Martin D, Donaldson M, Everett MA
Dept. Dermatology, Univ. Oklahoma, Health Sciences Center, 619 N.E. 13th, Oklahoma City, OK, 73104
J Cutan Pathol; 8(5):385-392 1981

The peroxidase-antiperoxidase technique was used to demonstrate a specific surface human T lymphocyte antigen (HTLA) in atrophic large plaque parapsoriasis. Tissue specimens obtained from a 55-yr-old man with a 6-yr history of parapsoriasis were prefixed in paraformaldehyde before freezing, treated with anti-HTLA, and examined by transmission electron microscopy. Positive membranous staining indicating the presence of HTLA was observed in 70% of cells. A high proportion of cells had convoluted nuclei; approx 80% of cells with convoluted nuclei were HTLA positive. The findings suggest a relationship between the atrophic large plaque parapsoriasis and mycosis fungoides. (27 Refs)

OTHER RELATED STUDIES

32. NEUROENDOCRINE DIFFERENTIATION IN BASAL CELL CARCINOMAS.

Dardi LE, Memoli VA, Gould VE
(c/o Gould) Dept. Pathology, Rush-Presbyterian-St. Luke's Medical Center, 1753 West Congress Parkway, Chicago, IL, 60601
J Cutan Pathol; 8(5):335-341 1981

Ten consecutive cases of basal cell carcinomas were reviewed. Nine of these displayed the typical histology of basal cell carcinoma, the other case was composed of small spindle to ovoid cells with scant cytoplasm and a high mitotic rate, resembling an 'oat cell' carcinoma. These were studied using the immunoperoxidase technique for tissue localization of calcitonin, insulin, glucagon, somatostatin, ACTH, gastrin and nerve growth factor. Three cases were negative for all hormones tested. Three cases were focally positive for a single hormone; one each for calcitonin, somatostatin, and ACTH. Two cases were focally positive for ACTH and somatostatin and two cases were focally positive for calcitonin, somatostatin and ACTH. None of the other hormones displayed activity. The positive staining was eliminated after absorption by the specific antigen. This immunohistochemical study illustrated neuroendocrine differentiation in basal cell carcinomas as has previously been suggested by the Grimelius stain and electron microscopy. Thus, as demonstrated in other epithelial neoplasms, basal cell carcinoma may also display neuroendocrine differentiation. This illustrates the potential multidirectional differentiation in neoplastic epithelial cells. (Author abstract) (23 Refs)

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DETECTION/ CHARACTERIZATION/ ISOLATION

1. DOUBLE LABELED-ANTIGEN METHOD FOR DEMONSTRATION OF INTRACELLULAR ANTIGENS IN PARAFFIN-EMBEDDED TISSUES.

Falini B, De Solas I, Halverson C, Parker JW, Taylor CR
Istituto di Clinica Medica Generale et Terapia Medica, Universita di Perugia, Policlinico, Monteluce, 0611 Perugia, Italy
J Histochem Cytochem; 30(1):21-26 1982

A double 'labeled-antigen' method has been developed for the simultaneous staining of both kappa and lambda light chains in fixed paraffin sections. The method is a two step procedure utilizing a mixture of antisera against kappa and lambda light chains in the first stage, followed by the addition of a mixture of kappa antigen labeled with horseradish peroxidase and lambda antigen labeled with alkaline phosphatase. The selection of substrates yielding reaction products of contrasting color enabled the observer to distinguish kappa-containing cells (brown) from lambda-containing cells (blue). Reactive plasma cells stained either pure brown (kappa) or clear blue (lambda) in a ratio of 1.5:1. Blood vessels containing serum immunoglo-

HE 20.3173/2:

bulins showed a mixed brown-blue reaction, as did the Reed-Sternberg cells of some cases of Hodgkin's disease. The advantages of this double labeled-antigen method over previously reported methods for achieving double staining are discussed. (Author abstract) (31 Refs)

2. PURIFICATION OF HUMAN TUMOR NUCLEOLAR ANTIGENS TO ELECTROPHORETIC HOMOGENEITY.

Chan PK, Busch RK, Takahashi K, Busch H
Dept. Pharmacology, Baylor Coll. Medicine, Houston, TX, 77030
Transplant Proc; 13(4):1955-1957 1981

Affinity chromatography and preparative isoelectric focusing were use to isolate human tumor nucleolar antigens in electrophoretically homogeneous states. Purity of the antigens was analyzed by two-dimensional gel electrophoresis. The major antigen (mol wt approx 54,000 daltons) focused at approx pH 6.3 (two spots). The minor antigen (mol wt approx 50,000 daltons) focused at pH 6.1. The major antigens were separated from the minor antigen by preparative isoelectric focusing with a recovery of approx 80%. V8 protease digestion of the antigen produced several peptides. The major antigen (54/6.3) was first cleaved into a smaller peptide with mol wt 50,000 daltons, and was further cleaved into two peptides with mol wt 32,000 and 18,000 daltons. Peptides of similar size but in different concentrations were observed in the V8 protease digest of the minor antigen. Importance of detection of the antigens for cancer diagnosis is discussed. (10 Refs)

3. CHEMICAL STUDIES OF TISSUE POLYPEPTIDE ANTIGEN (TPA). III. ON THE NATURE OF THE ANTIGENIC DETERMINANT(S) OF TPA SUBFRACTION B1.

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Acta Chem Scand [B]; 35(5):325-336 1981

Tissue Polypeptide Antigen (TPA) which is a protein isolated from human carcinoma cells, has previously been separated into subfractions and studied with biochemical methods. Gel diffusion studies show that the antigenic determinants are retained through the isolation and purification procedures. Specific modifications of the amino acid residues lysine, tyrosine, tryptophan and arginine in subfraction B1 have been related to the change in the capacity of the antigen to bind to horse anti-HeLa serum. Complete although reversible loss of binding capacity resulted from blocking of arginine and a minor loss was noted upon modification of tyrosine. No measurable influence was noted upon modification of lysine or tryptophan. No cysteine has been detected in subfraction B1. Circular dichroism measurements show that TPA subfraction B1 is largely alphahelical in solution, and that no correlation could be detected between antigenic activity and conformation. (Author abstract) (33 Refs)

4. IMMUNOLOGICAL AND CYTOCHEMICAL IDENTIFICATION OF HUMAN LEUKAEMIC PROMEGAKARYOBLAST (MEETING ABSTRACT).

Vainchenker W, Deschamps FJ, Xu FX, Bastin C, MacMicheal A, Breton-Gorius J
Hopital Henri Mondor, 94010 Creteil, France
Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Murine small megakaryocyte (MK) precursor ie promegakaryoblast (PMKB) can be identified by the presence of acetylcholinesterase activity which is specific for MK line. Human MK lack this enzyme and PMKB remain undetectable even at electron microscope (EM). Some yr ago, we have shown that platelet peroxidase (PPO) which is specific for MK-platelet line can be used to recognize normal and leukemic PMKB. PPO which is only dectected by EM cytochemistry is present in endoplasmic reticulum of small cells with a lymphoid morphology and without specific MK organelles. We presently report another marker of PMKB detected by immunological techniques. Antigens on membrane platelets were used to produce monoclonal antibodies. One of them, J15 stains after indirect immunofluorescence MK and some small cells. We observed that these labelled cells also possess PPO. The simultaneous revelation of PPO and platelet antigen by an indirect method at EM level has shown that all small cells labelled by J15 possess PPO. However some PMKB identified by PPO remained unlabelled by J15. Thus, this monoclonal antibody provide a new method to identify at light microscopic level, a part of PMKB. (no Refs)

5. FURTHER BIOCHEMICAL CHARACTERIZATION OF THE HUMAN THYMOCYTE DIFFERENTIATION ANTIGEN T6.

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J Immunol; 128(1):426-432 1982

Charge heterogeneity of the human thymocyte antigen T6 was studied by isoelectric focusing and two-dimensional gel electrophoresis. The larger subunit of T6 (a 49,000 mol wt glycoprotein) contained several oligosaccharide side chains bearing up to 12 terminal sialic acids. When T6 antigens from 19 individual thymuses were analyzed, no differences in the isoelectric focusing patterns of the larger subunit could be detected. The larger subunit of the T6 antigen from MOLT-4 cells (52,000 mol wt) contained an extra oligosaccharide if compared with the T6 antigen from thymus or three other T leukemic cell lines. Two types of small subunits of T6 were found. In addition to a protein of mol wt 12,000, pI 5.5 identified as beta2-microglobulin, a (mol wt 12,000, pI 7.0) nonglycosylated protein, was detected on two dimensional gels. This protein does not cross-react with beta2-microglobulin, and its amount varied in different T6 preparations. The tissue distribution, the mol wt the association with beta2-microglobulin and the limited structural heterogeneity of T6 support the idea that T6 is the human homologue of the murine thymus leukemia antigen (TL). (Author abstract) (36 Refs)

6. THE REACTION SPECIFICITY OF VARIOUS MONOCLONAL ANTIBODIES AND CELLULAR ORIGIN AND DIFFERENTIATION OF CULTURED CELL LINES DERIVED FROM HUMAN LEUKEMIAS AND LYMPHOMAS.

Tobinai K, Hirose M, Minato K, Shimoyama M
(c/o Shimoyama) Section Hematology, Natl. Cancer Center Hosp., 1-1, Tsukiji 5-chome, Chuo-ku, Tokyo 104, Japan
Jpn J Clin Oncol; 11(3):469-479 1981

Human hemopoietic tumor-cell lines (6 T-cell; 10 B-cell; 5 non-T, non-B-cell; 2 myeloid; 2 monocytoid) were grown exponentially, and their reactions to 12 monoclonal antibodies (OKT 3, OKT 4, OKT 6, OKT 8, OKI 1, OKM 1, anti-Leu-1, 10.2, (antihuman Lyt 2), 9.6 (antihuman Lyt-3), anti-B1, J5, anti-Mo 1) were evaluated by indirect immunofluorescence assay and by rosette-forming capacity with sheep erythrocytes, human T-lymphocyte antigen, Ia-like antigen, and surface immunoglobulins. The reactivities of the monoclonal antibodies were highly specific against cultured leukemia and lymphoma cell lines, with a few exceptions, which are described. The titer of the antibody differed among the cell lines, indicating that while use of the monoclonal antibodies specific for certain differentiation antigens may be useful for elucidating the cellular origin, stage of differentiation, and subset identification of human hemopoietic tumor cells, the titration of each monoclonal antibody requires the use of several cultured cell lines in order to determine an appropriate concentration for clinical use. (42 Refs)

7. MEGAKARYOCYTIC LEUKEMIA: IDENTIFICATION UTILIZING ANTI-FACTOR VIII IMMUNOPEROXIDASE.

Innes DJ, Mills SE, Walker GK
Dept. Pathology, Univ. Virginia Medical Center, Box 214, Charlottesville, VA, 22908
Am J Clin Pathol; 77(1):107-110 1982

Coagulation Factor VIII is produced by endothelial cells and megakaryocytes. Antibody directed against Factor VIII or its associated antigens has been shown to be a sensitive marker for both normal and neoplastic endothelial cells. It use to identify neoplastic megakaryocytes has not been described. We used immunoperoxidase localization of Factor VIII to identify megakaryocytes and immature megakaryocytic precursors in a case of megakaryocytic leukemia. (Author abstract) (14 Refs)

8. DETECTION OF AN ANTISQUAMOUS ANTIBODY IN MULTIPLE KERATOACANTHOMA.

Ahmed AR, Sofen H, Saxon A
Div. Dermatology, Univ. California Los Angeles Sch. Medicine, CHS 52-121, Los Angeles, CA, 90024
Clin Immunol Immunopathol; 22(1):20-31 1982

A case of multiple keratoacanthoma involving the skin and mucous membranes is reported. An antisquamous antibody was detected in the patient's serum which bound to a membrane antigen on squamous tumor cell lines COLO-16 and SCaBER. The approx mol wt of the antigen is 68,000. The antibody appears to be of the IgG class. It is possible that antibodies such as these may be directed toward neoplastic tissue and could play an important role in spontaneous tumor regression seen in patients with multiple keratoacanthoma. (Author abstract) (32 Refs)

9. TISSUE DISTRIBUTION, MOLECULAR PROFILE, AND SHEDDING OF A CYTOPLASMIC ANTIGEN IDENTIFIED BY THE MONOCLONAL ANTIBODY 465.12S TO HUMAN MELANOMA CELLS.

Natali PG, Wilson BS, Imai K, Bigotti A, Ferrone S
(c/o Ferrone) Dept. Pathology and Surgery, Coll. Physicians and Surgeons, Columbia Univ., New York, NY, 10032
Cancer Res; 42(2):583-589 1982

The mouse immunoglobulin G2 monoclonal antibody (MoAb) 465.12S reacts with a cytoplasmic antigen present in human melanoma cells but not detectable in melanocytes. Indirect immunofluorescent staining of a large number of surgically removed normal adult and fetal tissues with the MoAb 465.12S detected the cytoplasmic antigen in epithelial cells from several organs. The intensity of staining was greater in adult tissues than in the corresponding fetal tissues. Furthermore, the MoAb 465.12S stained nearly all of the surgically removed tumors tested but did not stain many of the normal tissues from which they originated. In almost all cases, the intensity and frequency of staining was greater for tumor cells than for corresponding normal tissues. From cultured carcinoma and melanoma cells, the MoAb 465.12S immunoprecipitated four glycopolypeptides with mol wt of 94,000, 75,000, 70,000, and 25,000. Incorporation of 3H-labeled sugars into the various components of the cytoplasmic antigen revealed that the MW 75,000 component was unusual in that it contained only glucosamine and mannose. The antigenic determinant defined by the MoAb 465.12S appears to be protein rather than carbohydrate in nature since it is heat sensitive and is expressed on the antigens synthesized by cells in presence of tunicamycin. Analysis of the spent culture medium of carcinoma and melanoma cell lines revealed that the cytoplasmic antigen is readily shed by these cells and consists of a major MW 94,000 and a minor MW 72,000 component. Treatment of cultured melanoma cells with the antibiotic tunicamycin showed that glycosylation of the cytoplasmic antigen is required for its shedding and/or stability in the spent culture medium. (Author abstract) (30 Refs)

10. HETEROGENEITY IN SURFACE ANTIGEN AND GLYCOPROTEIN EXPRESSION OF CELL LINES DERIVED FROM DIFFERENT MELANOMA METASTASES OF THE SAME PATIENT. IMPLICATIONS FOR THE STUDY OF TUMOR ANTIGENS.

Albino AP, Lloyd KO, Houghton AN, Oettgen HF, Old LJ
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
J Exp Med; 154(6):1764-1778 1981

Three melanoma cell lines (DX-1,-2, and-3) derived from separate metastatic foci of patient DX (a 70 yr old woman) were examined for phenotypic differences in growth, morphology, and expression of cell surface antigens and glycoproteins. DX-1 and-2 accumulated visible pigment; DX-3 cell appeared unpigmented. DX-2 and-3 cell lines grew as attached monolayers, while DX-1 showed a marked tendency to grow in suspension after initial attachment as microcolonies of rounded cells. Only DX-1 and-3 cells expressed D-locus human WBC antigen surface antigens. Less marked but characteristic differences were detected in the expression of other cell surface antigens. DX-2 and-3 exhibited similar profiles of cell surface glycoproteins in the high mol wt region, with 90,000 and 120,000 mol wt components being particularly prominent. DX-2 had an additional prominent component of 60,000 mol wt which was only weakly labeled in DX-3. DX-3 exhibited two major glycoproteins in the low mol wt region of 32,000 and 27,000. Only one major glycoprotein of 90,000 mol wt was labeled in DX-1 monolayer cells. Sera from patient DX reacted only with surface antigen of autologous DX-2; the highest reactivity was in the IgG fraction. The time-course of DX autologous reactivity was examined. Absorption analysis indicated that the DX-2 antigen was a class 1 melanoma antigen; the antigen was also detectable in much lower but demonstrable amounts in DX-1 and-3 cells. No other cell type tested exhibited the class 1 DX melanoma antigen. (21 Refs)

11. MONOCLONAL ANTIBODIES AGAINST SURFACE ANTIGENS OF LARYNGEAL CARCINOMA CELLS.

Zenner HP
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Arch Otorhinolaryngol; 233(2):161-172 1981

Production of monoclonal antibodies against laryngeal carcinoma (LC) cells is reported. BALB/c mice were immunized with LC cells of line HLaC78 (1 x 10(6)-5 x 10(7) cells x 2 at a 6-wk interval) or with cell membranes (CM) from LC cells.

Spleen cells were obtained 3 days after the second injection. Spleen cells were fused with mouse myeloma 653 cells to form antibody-producing cells capable of proliferation. A total of 1,882 clones of spleen cells were developed, including 1,102 from mice immunized with CM and 780 from mice immunized with intact cells (IC). Antibodies that bound to intact LC were produced by 73 clones, all from IC-immunized mice. Antibody from one clone was identified which bound malignant target cells, including two types of LC and two types of salivary gland tumor cells, but which did not bind normal fibrocytes, lymphocytes, or other normal human cell types, or nonhuman cells. The antibody, produced by hybridoma clone 1g6, was an IgG. Diagnostic potential of the IgG is described. (32 Refs) (In GER)

12. HYBRIDOMA MONOCLONAL ANTIBODY: USE IN DEFINING SURFACE ANTIGENS ON HUMAN LUNG CARCINOMA CELLS.

Kasai M, Saxton RE, Holmes EC, Burk MW, Morton DL, Bonnard, Alexander P, Ferrone S, Ivanyi P, Nathanson SD, Pious D, Embleton MJ
54-140 CHS, UCLA Sch. Medicine, Los Angeles, CA, 90024
Transplant Proc; 13(4):1942-1946 1981

Surface antigens on UCLA-SO-P3, the squamous cell lung carcinoma cell line derived from a 53-yr-old man, were compared with those on PL3, the autologous lymphoblast line obtained from the same patient. Using the autologous cell lines, two hybridomas were selected which secrete monoclonal antibodies that bind antigenic determinants present at high density on the carcinoma cells but not on the paired lymphoblastoid cells. The two cloned hybridomas, designated 169D4 and 169F3, were grown as ascites tumors in mineral oil-primed BALB/c mice. The two binding curves obtained by titration of hybridoma cells with P3 and PL3 target cells were compared. An end-point titer greater than 1:100,000 for both antibodies to the P3 carcinoma but only 1/:10 to PL3 for the 169D4 monoclonal antibody and 1:100 for 169F3 was revealed. The shapes of these antibody binding curves showed that the antigenic determinants recognized by the two monoclonal antibodies were present at high density on the P3 carcinoma but at low density or absent from the PL3. The immunoglobulin isotype of both 169D4 and 169F3 monoclonal antibodies was identified as IgM. The two monoclonal antibodies were tested for binding to 12 carcinoma cell lines, 9 melanoma, 2 sarcoma, 4 lymphoblast, and 1 human embryonic. Among the cell lines tested, only the lung carcinoma P3 and the colon carcinoma HT29 expressed detectable levels of 169D4 surface antigen. 169F3 monoclonal antibody recognized an epitope present on every human tumor cell line and on human embryo cells, but not on the lymphoblastoid cell lines. (6 Refs)

13. MONOCLONAL ANTIBODY AGAINST A1 LEWIS D ANTIGEN PRODUCED BY THE HYBRIDOMA IMMUNIZED WITH A PULMONARY CARCINOMA.

Iwaki Y, Kasai M, Terasaki PI, Bernoco D, Park MS, Cicciarelli J, Heintz R, Saxton RE, Burk MW, Morton DL
Dept. Surgery, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA, 90024
Cancer Res; 42(2):409-411 1982

A monoclonal antibody (CALed) against a human pulmonary squamous cell carcinoma line was cytotoxic to the line but did not react to an autologous B-lymphoblastoid line. Although the antibody was thought to be cancer specific, principally on the basis of this evidence, the antibody actually had the A1 Lewis d (Led) specificity. It reacted with approximately 2% of the random donor T-lymphocytes and with all six lymphocytes from donors who were A1 Led type without reacting to lymphocytes of any other type. The monoclonal antibody reactivity was also absorbed out by A1 Led red blood cells but not by red cells of other types. We conclude that the A1 Led antigen had been synthesized by the pulmonary carcinoma lines but not by the autologous lymphoblastoid line, resulting in disparity for this antigen. Since the combination A1 Led only occurs in 2% of the population, it is difficult to distinguish this type of antibody from tumor-specific antibodies. (Author abstract) (14 Refs)

14. TUMOR-ASSOCIATED CHROMATIN ANTIGENS OF HUMAN COLON ADENOCARCINOMA CELL LINES HT-29 AND LOVO.

Duhl DM, Banjar Z, Briggs RC, Page DL, Hnilica LS
Dept. Biochemistry, Vanderbilt Univ. Sch. Medicine, Nashville, TN, 37232
Cancer Res; 42(2):594-600 1982

Antiserum to dehistonized chromatin from human colon adenocarcinoma cell line HT-29 was raised in rabbits and used for the immunodetection of colon tumor-associated nuclear antigens. Quantitative microcomplement-fixation studies indicated that the antiserum had reactivity similar to those of chromatins of two human colon adenocarcinoma cell lines (HT-29 and LoVo) and with nonneoplastic colon. Immunocytochemical localization showed the chromatin antigens to be evenly dispersed throughout the nucleus. Immunochemical staining of electrophoretically separated chromosomal proteins transferred to nitrocellulose sheets revealed several intensely staining antigens predominantly in the mol wt range of 62,000 to 75,000. When the antiserum was immunoabsorbed with nonneoplastic human colon chromatin, two antigens with mol wt of 67,000 and 92,000 were identified only with the tumor chromatins. Antiserum immunoabsorbed with either LoVo or HT-29 chromatin failed to show any immunoreactivity, suggesting that these tumor-associated proteins, or antigenic sites residing on these proteins, are identical in both colon tumor cell lines. (Author abstract) (43 Refs)

15. IN VIVO LOCALIZATION OF HUMAN TUMOUR XENOGRAFTS BY RADIOLABELLED MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

Moshakis V, McIlhinney RJ, Raghavan D, Neville AM
Ludwig Institute for Cancer Research, Royal Marsden Hospital, London, England
Clin Oncol; 34(8):258 1981

The advantages of recently developed monoclonal antibodies offer the possibility of deriving reagents with a higher degree of tissue specificity. We have tested their localizing potential using human tumors grown as xenografts in immune-suppressed mice. A monoclonal antibody (LICR-LON-HT/13) has been raised to cell surface antigens expressed by a human malignant teratoma xenograft (HX39) and has been shown to bind to teratoma cells in vitro. Tumor-bearing mice were injected iv with equal amounts of 125I-labelled specific monoclonal antibody and 131I-labelled non-specific normal mouse IgG, simultaneously. Antibody localization in the tumor was examined at the cellular level by autoradiography. The tumor uptake of monoclonal antibody was 17-56 x higher than in normal tissues. The tumor/blood ratio increased from 0.3 at 4 hr post-injection to 10.2 at 96 hr. This preferential localization did not occur with control mouse IgG. The kinetics of localization were the same in six different experiments involving a total of 90 tumors. The same antibody localized in two human teratoma xenografts, but did not localize in a human breast carcinoma. Furthermore, another monoclonal antibody (LICR-LON-FIB75) that did not bind to human teratoma cells in vitro, failed to show localization in vivo. The degree of localization was related to tumor size; small tumors took up higher amounts of antibody per unit of wet wt than large tumors. This did not occur with the control IgG preparation. Autoradiography showed that the injected monoclonal antibody was localized to the viable parts of the tumors and in close association with the tumor cell surface. Monoclonal antibodies, therefore, are capable of localizing specifically in human tumor xenografts. It appears that they can achieve, at least in tumor xenografts, higher levels than conventionally raised antisera used to date. This propensity to localize preferentially in small tumors may be of value when the antibodies are used in clinical studies to detect micrometastases. (3 Refs)

16. ANTIGENS ON NATURALLY OCCURRING ANIMAL AND HUMAN TUMORS DETECTED BY MONOCLONAL ANTIBODIES.

Embleton MJ, Gunn B, Byers VS, Baldwin RW, Bonavida B, Martin WJ, Ferrone S
Cancer Res. Campaign Lab., Univ. Nottingham, Nottingham, NG7.2RD, England
Transplant Proc; 13(4):1966-1969 1981

Reactivities of monoclonal antibodies prepared against a spontaneously arising rat mammary carcinoma and human osteogenic sarcoma cells were studied. An antibody-secreting hybridoma was prepared by fusion of the mouse myeloma P3-NS1-Ag4 (P3NS1) with spleen cells from rats immunized against a syngeneic mammary carcinoma, Sp4. The monoclonal antibody produced reacted only with mammary carcinoma Sp4 and did not bind to other rat tumors or normal rat cells. Two cell lines (791T/36 and 791T/48) from hybridomas obtained by the fusion of spleen cells from BALB/c mice immunized with the 791T osteogenic sarcoma cell line with P3NS1 cells, produced antibody that reacted preferentially with 791T cells. Antibody 791T/36 reacted strongly with 791T cells and with another osteogenic sarcoma, 788T, and more weakly with two others, 805T and 845T; the antibody did not react with six other osteogenic sarcomas. Tests against 11 lines of cultured fibroblasts, including 3 lines derived from the donor of 791T and 2 from donors of cross-reactive sarcomas, were negative. Monoclonal antibody from 791T/48 gave different cross-reactions. Two different monoclonal antibodies to a human osteogenic sarcoma cell line reacted with the immunizing cell line but not with cultured fibroblasts from the tumor host. Neither showed specificities for blood group or D-locus antigens. Despite apparent tumor association, the antigens detected by the monoclonal antibodies were not shared by all osteogenic sarcomas and were not restricted to this tumor type. (10 Refs)

17. DETECTION OF HUMAN OSTEOSARCOMA-ASSOCIATED ANTIGEN(S) BY MONOCLONAL ANTIBODIES.

Hosoi S, Nakamura T, Higashi S, Yamamuro T, Toyama S, Shimomiya K, Mikawa H
Dept. Pediatrics, Univ. Kyoto, Sakyo-ku, Kyoto 606, Japan
Cancer Res; 42(2):654-659 1982

Hybrid cell lines have been derived from a fusion between mouse myeloma cells, NS1, and spleen cells from mice immunized with freshly resected osteosarcoma cells from an untreated patient. Of the 276 hybrids obtained, five secreted antibodies which bound to osteosarcoma tissues but not to autologous skin fibroblasts. The antibodies from three of these five hybrids, OST6, OST7, and OST15, reacted with all of five osteosarcoma tissues and with one chondrosarcoma tissue but not with other malignant or benign tumors. Tests of various normal tissues were negative, except for weak binding to a subpopulation of chondrocytes in articular cartilage. The reciprocal binding inhibition test showed that OST6, OST7, and OST15 antibodies were directed against different antigenic determinants. (Author abstract) (24 Refs)

18. SPECIFIC, ANTIGENIC PROTEIN OF GUERIN EPITHELIOMA.

Palka JA, Rzeczycki W
Inst. Biochemistry and Medical Analytics, Medical Acad., 15-230 Bialystok 8, Poland
Neoplasma; 28(5):527-532 1981

Specific, antigenic protein of the mol wt 61,000 and 66,000 and isoelectric point 5.15 were isolated from cytosol of Guerin epithelioma and antiserum against these proteins was obtained. These antigens appear to be specific for epithelioma. Such antigens were not found in any normal rat organ. Blood serum of Guerin epithelioma bearing rats does not contain antibodies against these antigens. (Author abstract) (19 Refs)

IMMUNOLOGICAL STUDIES

19. USE OF ANTIBODIES AGAINST TUMOR-ASSOCIATED ANTIGENS FOR CANCER DIAGNOSIS AND TREATMENT.

Ghose T, Ramakrishnan S, Kulkarni P, Blair AH, Vaughan K, Nolido H, Norvell ST, Belitsky P, Bonavida B
Dept. Pathology, Dalhousie Univ., Sir Charles Tupper Building, Halifax, Nova Scotia, Canada B3H 4H7
Transplant Proc; 13(4):1970-1972 1981

Antitumor effects of injections of methotrexate (MTX), adriamycin (ADR), and conjugates of MTX and ADR with antitumor globulin (ATG) were determined. Survival of C57BL/6J mice that had received free MTX or MTX conjugated to normal rabbit globulin (NRG) or ATG after ip injection of 10(4) EL4 lymhpoma cells/mouse is described. A dose of 15 mg/kg of free MTX and 3 mg/kg MTX, bound either to NRG or ATG, prolonged survival compared to that of untreated mice. Only MTX linked to ATG produced 'cell cure' in 2/10 mice. Survival of BALB/c mice that received 2 mg/kg of free ADR or 5 mg/kg of ADR linked to normal goat globulin (NGG) or ATG beginning 17 days after inoculation of 10(6) renal carcinoma cells/mouse is described. Although free ADR and ADR conjugated to NGG prolonged the survival of treated mice, only treatment with ADR-ATG conjugates led to long-term survival. When MTX was linked to NRG or ATG, its in vivo toxicity increased and the MTX-ATG conjugate was tumor-inhibitory at dose levels far below equimolar doses of free MTX. When ADR was linked to dextran-IgG, its toxicity was reduced: higher amounts of ADR could therefore be administered without producing a lethal toxic effect. The carrier role of such antitumor antibodies also was supported by the tumor-specific localization of a monoclonal antibody against human melanoma in metastatic lesions. Assay of radioactivity in mice with intracerebral transplants of the C1300 neuroblastoma revealed higher localization by antigen-binding (Fab2) fragments. The results suggested that monoclonal antitumor antibodies and their appropriate fragments are potentially useful for targeting radionuclides and antineoplastic agents. (3 Refs)

20. MONOCLONAL ANTIBODY-RICIN A CHAIN CONJUGATE SELECTIVELY CYTOTOXIC FOR CELLS BEARING THE COMMON ACUTE LYMPHOBLASTIC LEUKEMIA ANTIGEN.

Raso V, Ritz J, Basala M, Schlossman SF
Div. Pharmacology, Sidney Farber Cancer Inst., Boston, MA, 02115
Cancer Res; 42(2):457-464 1982

The toxic subunit of ricin has been conjugated by a disulfide bone to a monoclonal murine antibody (J-5) specific for the common acute lymphoblastic leukemia antigen (CALLA) expressed on human lymphoblastic leukemia cells. Both the monoclonal antibody and ricin A chain retained their original biological activity after conjugation. The ricin A chain antibody-combining site attached to the membrane of CALLA-bearing cells, whereupon both components of the molecule, antibody and A chain, could be detected using fluorescein-labeled antibody probes directed against either mouse F(ab')2 or ricin A chain. This conjugate proved to be a potent cytotoxin for CALLA-positive Nalm-1 cells growing in vitro and produced 50% inhibition of proliferation at levels of 2 x 10(-10) M. CALLA-negative cell lines were unaffected until levels of conjugate approached 10-6 M. When tested for cytotoxic action on Nalm-1 cells, the composite conjugate molecule was at least 2,000x more effective than J-5 antibody alone, ricin A chain alone, or a noncovalent mixture of these components. Cytotoxicity of the conjugate could be blocked completely by addition of antibodies specific for either mouse Ig or ricin A chain. Direct comparison of the in vitro cytotoxity of CALLA-directed univalent Fab versus bivalent F(ab')2 carriers of ricin A chain revealed 70-fold greater efficacy for the latter conjugate. This differential could not be accounted for by differences in A chain activity or binding affinity for the cell membrane but appeared related to the ability of the multivalent agent to induce modulation and internalization of CALLA determinants. No overt toxic effects were noted when the F(ab')2-A chain conjugates was administered iv to rabbits at levels as high as 20 mg/kg single injection or 5 mg/kg for 5 days. The unique specificity characteristics and high potency of this cytotoxic conjugate indicate that it has significant therapeutic potential for the treatment of CALLA-bearing human leukemias and lymphomas. (37 Refs)

21. ANALYSIS OF THE PEANUT AGGLUTININ-BINDING SITE AS A DIFFERENTIATION MARKER OF NORMAL AND MALIGNANT HUMAN LYMPHOID CELLS.

Galili U, Galili N, Or R, Polliack A
Dept. Haematology, Hadassah Univ. Hosp., Jerusalem, Israel
Clin Exp Immunol; 43(2):311-318 1981

Human lymphoid cells obtained from bone marrow, thymus, spleen, and lymph node tissues were studied for their capacity to bind fluorescein-bound (FITC) peanut agglutinin (PNA). The PNA-binding capacity of a variety of leukemic and cultured human lymphoblastoid cells was examined to determine if this membrane characteristic can be used to distinguish subsets of leukemic cells. Of normal cells from lymphoid organs studied, only thymocytes bound PNA. Peripheral blood lymphocytes did not bind PNA. RBC E-rosetting thymocytes bound PNA, whereas prothymocytes that did not form E rosettes did not bind PNA. Fetal splenic lymphocytes, like their adult counterparts, lacked PNA-binding capacity. Lymphoblastoid cell lines were examined for staining with FITC PNA. The only T-derived line that exhibited strong PNA binding was acute lymphoblastic leukemia (ALL)-derived Be13 cells. Hodgkin's disease-derived HD-MAR cells that readily form E rosettes interacted very weakly with PNA. Other T lines that express human T antigen lacked PNA-binding ability. All B cell-derived cell lines originating from African or American type Burkitt lymphoma exhibited strong specific binding of FITC-PNA. Other B-cell lines also exhibited PNA binding. Leukemic cells from 3/15 ALL patients, 3/3 with non-Hodgkin's lymphoma, and 1/1 with hairy cell leukemia exhibited PNA binding. Cells from 3/11 acute myeloid leukemia patients showed partial PNA binding. No leukemic cells from patients with chronic lymphocytic (9 patients) or chronic myeloid (4) leukemia bound FITC PNA. The usefulness of PNA as a differentiation marker in malignant cells is discussed. (31 Refs)

22. IDENTIFICATION OF NEURAL AND ADRENAL MEDULLARY SURFACE MEMBRANE GLYCOPROTEINS RECOGNIZED BY ANTISERA TO CULTURED RAT SYMPATHETIC NEURONS AND PC12 PHEOCHROMOCYTOMA CELLS.

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Dept. Neuropathology, Univ. Pennsylvania, Phila., PA, 19104

Neuroscience; 6(12):2773-2786 1981

The distribution of glycoproteins in the nervous system and recognized by antisera prepared against cultured rat sympathetic neurons and PC12 pheochromocytoma cells cultured with or without nerve growth factor (+ or-3 NGF) was examined. Antisera prepared against cultured PC12 cells and rat sympathetic neurons recognized a limited number of membrane glycoproteins. Species of glycoproteins recognized by the antisera were qualitatively similar. PC12-and PC12+ antisera immunoprecipitated the same group of fucosylated components. Components included the four recognized by antisera to rat sympathetic neurons. A close qualitative similarity between the antigenic glycoproteins present on PC12+ cells and PC12-cells and on rat sympathetic neurons was observed. NGF greatly increased the relative amount of a trypsin-sensitive, fucose- and glucosamine- containing component, termed NGF-inducible large external (NILE) glycoprotein. Results suggest that rat sympathetic neurons synthesize a material closely resembling NILE glycoprotein. (24 Refs)

23. EXPRESSION OF THY1, TL AND LYT ANTIGENS ON SPONTANEOUS LEUKEMIAS OF BALB/MO STRAIN OF MICE.

Strzadala L, Opolski A, Kisielow P

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Arch Immunol Ther Exp (Warsz); 29(4):439-441 1981

The expression of Thy1, and Lyt antigens on spontaneous BALB/Mo leukemias has been studied. The results obtained thus far indicate that a majority of leukemias express TL antigen and differentiated Lyt phenotype. This observation and other findings demonstrating and existence of TL+ thymocytes with different Lyt phenotypes in normal thymus of young mice lends support for the hypothesis that TL+Lyt2+ phenotype defines this stage in the T cell differentiation pathway, which is particularly sensitive to leukemic transformation. (Author abstract) (6 Refs)

24. USE OF CAPILLARY TUBE LEUKOCYTE ADHERENCE INHIBITION FOR THE DETECTION OF TUMOR-SPECIFIC IMMUNE RESPONSE.

Myers WL, O'Keefe ML
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Immunol Commun; 10(4):407-416 1981

The tumor-specific immune response of A/J mice was determined at various times after subcutaneous injection with a transplantable spindle-cell sarcoma (SaI) using a leukocyte adherence inhibition (LAI) assay carried out in capillary tubes. Solubilized antigens prepared by 3M KCl extraction of the specific tumor, other transplantable tumors and normal A/J liver were used in the evaluation of LAI reactivity. The assay was found to be capable of detecting a significant antitumor response before the subcutaneous tumors became detectable by palpation. The response remained significant until the tumors were greater than 25 mm in diameter. Responsive cell populations did produce an active supernatant, indicating the possible presence of a lymphokine and/or specific cytophilic antibody. (Author abstract) (19 Refs)

VIRUS ASSOCIATED ANTIGENS

25. DETECTION BY RADIOIMMUNOASSAY OF ANTIGENS RELATED TO THE P30 POLYPEPTIDES OF PRIMATE TYPE C ONCOVIRUSES IN PERIPHERAL LEUKOCYTES FROM PATIENTS WITH CHRONIC MYELOGENOUS LEUKAEMIA.

Toth FD, Vaczi L, Kiss J, Rethy A, Kiss A, Rak K
Inst. Microbiology, Univ. Medical Sch., 4012 Debrecen, Hungary
Acta Virol (Praha); 25(6):376-380 1981

Leukocytes from patients with chronic myelogenous leukemia were examined for antigens related to the p30 polypeptides of baboon endogenous virus (BaEV) and gibbon ape leukemia virus (GaLV). Samples from patients with the quiescent phase of the disease proved to be negative or contained p30 of BaEV as the only viral antigen. In cases of blastoid crisis or acceleration, an antigen related to p30 of GaLV could be detected. In five of six patients, acceleration or blastoid crisis was preceded by expression of GaLV p30. (Author abstract) (15 Refs)

26. SYNTHESIS OF A VIRAL PROTEIN WITH MOLECULAR WEIGHT OF 30,000 (P30) BY LEUKEMIC CELLS AND ANTIBODIES CROSS-REACTING WITH SIMIAN SARCOMA VIRUS P30 IN SERUM OF A CHRONIC MYELOID LEUKEMIA PATIENT.

Derks JP, Hofmans L, Bruning HW, Rood JJ
Dept. Immunohematology, Bloodbank, Univ. Hosp., Building 23, Rijnsburgerweg 10, 2333 AA Leiden, The Netherlands
Cancer Res; 42(2):681-686 1982

We studied a patient with a Philadelphia chromosome-positive chronic myeloid leukemia, who died in relapse after multiple transfusions and grafting with bone marrow from his monozygotic twin brother (referred to as 'donor' in this paper). We present data indicating that this patient may have had a retrovirus infection and that this virus is related to the group of exogenous primate Type C retroviruses. Antibodies to simian sarcoma virus (SSV) mol wt 30,000 protein (p30) but not endogenous feline virus RD-114 could be found in patient but not donor serum. Patient but not donor cells were able to actively synthesize a p30 protein that could be precipitated with patient serum and rabbit anti-SSV p30 but not with donor serum or rabbit anti-RD-114 p30. Patient p30 resembles SSV p30 but not RD-114 p30 in peptide mapping by limited proteolysis and subsequent slab gel electrophoresis. Patient but not donor cells were able to actively synthesize a mol wt 78,000 protein that could be precipitated with goat anti-SSV. An enzyme with properties of reverse transcriptase was increased 30-fold in patient cells when compared with donor and other control cells. Related to the presence of widespread infectious agents may be the finding that, in the course of the patient's disease, donor serum showed increasing amounts of possibly immunoregulatory antibodies, reactive with autologous and, more effectively, with patient-derived cell membrane mol wt 80,000 protein (a possible idiotypic receptor structure) and mol wt 94,000 protein (a T-cell alloantigen). (Author abstract) (31 Refs)

27. PRIMARY HEPATOCELLULAR CARCINOMA -- ETIOLOGY, PATHOGENESIS, AND PREVENTION.

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Inst. for Cancer Res., Fox Chase Cancer Center, Philadelphia, PA, 19111
Hum Pathol; 12(12):1085-1097 1981

Worldwide, primary hepatocellular carcinoma may be the most common cancer in men. Usually it occurs in association with cirrhosis or chronic hepatitis. In this article I present evidence that the majority of these cases are associated with, and probably caused by, persistent infection with hepatitis B virus. I also propose a model that describes the role of the hepatitis B virus in the pathogenesis of primary hepatocellular carcinoma. If persistent infection with hepatitis B virus is required for the development of most cases of primary hepatocellular carcinoma, prevention of such infections should prevent most cases of primary hepatocellular carcinoma. A vaccine against hepatitis B virus, prepared from surface antigen particles (HBsAg) harvested from the blood of hepatitis B virus carriers, has been safe and effective in preventing acute infection with hepatitis B virus in adult homosexual men. If it is equally safe and effective in young children, it will be administered widely to populations living in areas endemic for hepatitis B virus infections. Thereafter it may be possible to learn within 5 to 10 years whether the vaccine prevents chronic liver disease. If it does, it will be reasonable to conclude that it will also prevent primary hepatocellular carcinoma. (Author abstract) (47 Refs)

28. A CONTROLLED STUDY OF HEPATITIS CORE ANTIBODY (HBCAB) IN PRIMARY HEPATOCELLULAR CARCINOMA AND LIVER CIRRHOSIS IN KENYA.

Bowry TR, Shah MV, Ahmad Z
Immunology Section, Dept. Human Pathology, Univ. Nairobi, Nairobi, Kenya
East Afr Med J; 58(8):576-582 1981

Incidence of hepatitis B virus (HBV) markers was studied in 75 Kenyan patients with confirmed liver disease. Among these patients, 15 had liver cirrhosis (LC), 13 had LC and concomitant primary hepatocellular carcinoma (PHC), and 47 had PHC. Presence of hepatitis B surface antigen (HBsAg) was detected in 40% of the patients with LC, in 47% of the patients with LC + PHC, and in 46% of the patients with PHC. Among the HBsAg-positive patients, high titers of hepatitis B core antibody (HBcAb) were detected in 100% of the patients with LC, 100% of those with LC + PHC, and 90% of those with PHC. HBcAb as a sole marker of HBV was detected in

13% of the patients with LC, 31% of those with LC + PHC, and 9% of those with PHC. (16 Refs)

29. ANTICOMPLEMENT IMMUNOENZYMATIC METHOD OF DETECTING EPSTEIN-BARR NUCLEAR ANTIGEN IN NASOPHARYNGEAL CARCINOMA CELLS IN NORMAL EPITHELIAL CELLS.

Zeng Y, Shen S, Pi G, Ma J, Zhang Q, Zhao M, Dong H
Inst. Virology, Chinese Acad. Medical Sciences, Beijing, People's Republic of China
Chin Med J [Engl]; 94(10):663-668 1981

Epstein-Barr nuclear antigen (EBNA) was tested for by both anticomplement immunofluorescence and anticomplement immunoenzymatic (ACIE) methods in nasopharyngeal cells from 79 patients with nasopharyngeal carcinoma (NPC), cells from 66 patients with suspected NPC, cells from head and neck tumors other than NPC (18), and cells from the nasopharyngeal mucosa of 3-8 mo old dead fetuses (21). ACIE studies of exfoliated cells indicated NPC in 79 cases, of which 62 were also NPC-positive upon histologic and cytologic examination, 10 were NPC-positive by histologic examination only, and 7 were NPC-positive by cytologic examination only. Nine of the suspected cases were NPC-positive by the ACIE method, but were negative upon cytologic or histologic examination. None of the head neck tumor smears or fetal mucosa cells were NPC-positive by any method used. The findings of EBNA in carcinoma cells, hyperplastic epithelial (HE) cells, and ciliated columnar epithelial (CCE) cells of NPC patients, and in HE cells and CCE cells of normal individuals, but with less found in squamous epithelial cells, suggest that Epstein-Barr virus infects normal epithelial cells first, especially CCE cells, integrating its DNA into cellular DNA. (11 Refs)

30. VULVAR INTRAEPITHELIAL NEOPLASIA: CORRELATION OF NUCLEAR DNA CONTENT AND THE PRESENCE OF A HUMAN PAPILLOMA VIRUS (HPV) STRUCTURAL ANTIGEN.

Crum CP, Braun LA, Shah KV, Fu YS, Levine RU, Fenoglio CM, Richart RM, Townsend DE
Div. Ob/Gyn Pathology, Columbia Univ. Coll. of Physicians and Surgeons, 630 West 168th St., New York, NY, 10032
Cancer; 49(3):468-471 1982

Immunoperoxidase localization of a human papilloma virus structural antigen (HPV) was attempted in 68 intraepithelial lesions of the vulva, 39 of which were analyzed for nuclear DNA content by microspectrophotometry. Overall, 5.9% (4/68) stained positive for HPV. Ninety per cent (35/39) of the cases tested were aneuploid, and, of these, 2.8% (1/35) stained positive for HPV. In contrast, 50% (2/4) of the polyploid lesions were positive. Hence DNA microspectrophotometry and immunoperoxidase localization of HPV are useful coparameters for distinguishing wart virus infection (condylomata) from vulvar intraepithelial neoplasia. HPV is detected infrequently within aneuploid lesions, in keeping with the concept that epithelial maturation is required for virion assembly. Whether the HPV genome exists in a nonreplicative state within the aneuploid cell population is unknown. (Author abstract) (18 Refs)

31. POLYOMA T ANTIGENS.

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Adv Cancer Res; 35:1-25 1981

Current knowledge on polyoma T proteins is reviewed, including the role of these viral-coded proteins in lytic infection of mouse cells, DNA nucleotide sequences (coding and regulatory signals), mutations affecting the T antigens, and cell transformation and tumorigenicity. The T antigens are compared structurally with SV40 in terms of nucleotide sequences. The roles of the large, small, and medium T antigens in lytic infection and transformation are discussed. The functions associated with small and medium T antigens, particularly attempts to detect protein kinase activity associated with polyoma T, are reviewed. (110 Refs)

32. INTERACTION OF SV40 T-ANTIGEN WITH CHROMATIN IN TUMOR CELLS.

Rheszowska-Wolny I, Sadzinska L, Grobner S, Shliankevich MA, Drize OB, Demina EB, Polotskaia AV
Inst. Oncology, Gliwice, Poland
Biokhimiia; 46(10):1880-1886 1981

Sedimentation analysis and electrophoresis in the polyacrylamide gel showed the presence of T-antigen of simian virus SV40 in the chromatin isolated from SV40-induced Syrian hamster tumors. T-antigen was bound to oligonucleosomes fraction. It was suggested that T-antigen interacts not only with DNA but also with H1 histone. (24 Refs) (In RUS)

TUMOR ASSOCIATED TRANSPLANTATION ANTIGENS

33. DECREASED LEVELS OF CIRCULATING LYTIC ANTI-T IN THE SERUM OF PATIENTS WITH METASTATIC GASTROINTESTINAL CANCER: A CORRELATION WITH DISEASE BURDEN.

Bray J, Maclean GD, Dusel FJ, McPherson TA
Dept. Medicine, Cross Cancer Inst., 11560 University Ave., Edmonton, Alberta, T6G 1Z2, Canada
Clin Exp Immunol; 47(1):176-182 1982

Using a cytotoxicity assay, we have shown that all of 40 normal human sera tested contained antibodies cytotoxic for neuraminidase-treated red blood cells in the presence of complement. The antibodies were shown to be specific for the T disaccharide by studies using a synthetic T antigen. Certain patients with metastatic gastrointestinal cancer were found to have depressed serum levels of anti-T when compared to normal controls. There was a correlation between depression of circulating anti-T and disease burden in that 83% of patients with extensive disease had lower than normal levels of cytotoxic anti-T as compared to 45% of patients with moderate disease and none with minimal disease. There was no correlation between the concentration of cytotoxic anti-T and the age of the patients, time since surgery or the type of therapy the patient was receiving. Patients with low levels of cytotoxic anti-T had normal levels of cytotoxic anti-sheep red blood cell antibody. Measurement of circulating anti-T in the serum of certain cancer patients may prove valuable in the monitoring of disease progression. (Author abstract) (23 Refs)

34. ADCC OF CULTURED HUMAN MELANOMA CELLS: ANALYSIS WITH MONOCLONAL ANTIBODIES TO HUMAN MELANOMA-ASSOCIATED ANTIGENS.

Imai K, Ng AK, Glassy MC, Ferrone S

Dept. Molecular Immunology, Scripps Clinic and Res. Foundation, La Jolla, CA

Scand J Immunol; 14(4):369-377 1981

Four monoclonal antibodies to human melanoma-associated antigens (MAA) were found to be able to mediate specific cell-dependent lysis (ADCC) of cultured human melanoma cells. The extent of specific lysis of melanoma cells was influenced by the effector to target cell ratio, the amount of antibody added to the reaction mixture, and the incubation time. Cultured melanoma cells treated for 16 hr with puromycin or cycloheximide (final concentration, 1.0 ug/ml) displayed increased susceptibility to ADCC even though the cell surface expression of MAA was not changed. On the other hand, treatment of melanoma cells with tunicamycin (final concentration, 1.0 ug/ml) reduced the expression of MAA but did not affect susceptibility to ADCC. These findings suggest that other properties of the target cell membrane besides antigen density play a role in the outcome of ADCC reaction. (Author abstract) (16 Refs)

35. EXPRESSION OF HERPES SIMPLEX VIRUS COMMON SURFACE ANTIGENS AND MALIGNANCY BY CLONAL CELLS OF A HERPES SIMPLEX VIRUS TYPE 2-TRANSFORMED LINE.

Kimura S, Okazaki K, Tanaka S, Yoshida N

Dept. Microbiology, Kochi Medical Sch., Oko-cho, Nankoku-shi, Kochi-ken 781-51, Japan

Gan; 72(6):834-841 1981

Herpes simplex virus (HSV) type common surface antigens (CSA) were examined by indirect immunofluorescence with rabbit antiserum to HSV Type 1 in a clonal hamster cell line 155-4 transformed by HSV Type 2. The tumor formation was examined in hamsters transplanted with various transformed and tumor cells. The examination of subclones derived from 155-4 cell line gave the following results. (1) Thirty subclones were isolated and classified into three phenotypes as to CSA expression: (i) in CSA-positive type (20% of the clones isolated), the number of CSA-positive cells increased soon (5 hr) after seeding at 37 C; (ii) in CSA-inducible type (33% of the clones), the number of CSA-positive cells increased after treatment with actinomycin D (ACT-D, 2 ug/ml), but not without ACT-D; (iii) in CSA-negative type (47% of the clones), the number of CSA-positive cells did not increase after seeding or after ACT-D treatment. (2) In tumor cell lines derived from the parent line and from three representative clones, CSA expressions were similar to that by CSA-negative type. (3) Transformed cells expressing CSA after seeding or after ACT-D treatment formed tumors and metastases less efficiently than cells expressing little CSA in transplanted hamsters. (4) Tumor cell lines formed tumors and metastases more efficiently than transformed cells expressing little CSA in tran splanted hamsters. (Author abstract) (17 Refs)

36. ANTITUMOR IMMUNITY INDUCED BY LIPOSOMES SENSITIZED WITH A SOLUBLE TUMOUR ANTIGEN (MEETING ABSTRACT).

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UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Results obtained in a syngeneic rat lymphoma have shown that the association of tumor cell surface associated proteic antigen with liposomes has a good adjuvant effect on the antibody response. The requirements for the expression of this adjuvant effect were further analyzed regarding the source of antigen, the need of macrophage stimulating agent, the association with lipids and the lipids composition. 1) When whole cells or cytosol were used as source of soluble antigen, a significant adjuvant effect of liposome presentation was observed whereas antigen solubilized from cell membranes was unsuitable. 2) Adjuvant effect of liposome presentation is depending on presence of a chemotactic product: liposomes showed adjuvant effect only when mixed with complete or incomplete Freund Adjuvant; no adjuvant effect was observed when live BCG microorganisms were used; moreover, in the absence of Freund Adjuvant liposomes containing a powerful chemotactic tripeptide showed a significant adjuvant effect. 3) The soluble antigen must be associated with the lipids since injection of soluble antigen and empty liposomes mixed in complete Freund Adjuvant was not followed by a significant antibody response. 4) Nature of phospholipids used to make liposomes may be of importance: liposomes made from dipalmitoylphosphatidylcholine or sphyngomyeline or egg lecithines showed strong adjuvant effect, whereas liposomes made from dimyristoylphosphatidylcholine did not. (no Refs)

37. THE IMMUNOGENIC AND TUMORIGENIC PROPERTIES OF A MURINE LYMPHOMA THAT EXPRESSES FOREIGN ALLOANTIGENS: ROLE OF HELPER FACTOR(S) IN GENERATING A CYTOTOXIC RESPONSE IN VITRO.

Scott JW, Finke JH, Carrido F, Rogers MJ, Bonavida B, Bonnard, Ivanyi P, Schirrmacher V

Dept. Immunology, Res. Div., Cleveland Clinic Foundation, Cleveland, OH, 44106

Transplant Proc; 13(4):1867-1873 1981

Mice of haplotypes that did (SJL, BALB/c, and C57BL/6) and did not (C3H/He) share antigens expressed on CH-1 cell line were selected, and the in vitro cytotoxic responses of the various haplotypes against CH-1 and the growth of CH-1 in vivo were examined. CH-1 was not tumorigenic in SJL, C57BL/6, or C3H/He mice. These strains generated a strong cytotoxic response against CH-1. CH-1 was lethal when injected into BALB/c mice. BALB/c responder cells generated only a weak in vitro cytotoxic response against CH-1. Potentiation of the BALB/c anti-CH-1 cytotoxic response by helper factors was investigated. The addition of helper supernates resulted in a threefold increase in percent specific lysis when compared with effectors generated in the absence of added helper factor. This increase in cytotoxic activity was observed at all three effector-to-target cell ratios tested. Deletion of nylon wool adherent cells from the responding population eliminated the development of a detectable cytotoxic response. Cytotoxic T lymphocytes specific for CH-1 were generated from nylon wool nonadherent cells when helper factor was provided during the sensitization phase. The generation of cytotoxic effector cells was dependent on helper factor and antigen stimulation. Helper factors induced by either bacterial antigens or cell-bound alloantigens assisted the development of specific effector cells. (16 Refs)

38. IMMUNOTHERAPY OF A MURINE COLON CANCER WITH SYNGENEIC SPLEEN CELLS, IMMUNE RNA AND TUMOR ANTIGEN.

Fukushima M, Colmerauer ME, Nayak SK, Koziol JA, Pilch YH
1st Dept. Surgery, Hirosaki Univ. Sch. Medicine, Hirosaki, Japan
Int J Cancer; 29(1):107-112 1982

In combination with xenogeneic immune RNA (I-RNA) and tumor antigen (TA), syngeneic spleen cells inhibited the growth of a N-methyl-N-nitrosourethane-induced colon carcinoma (CT-26) in BALB/c mice. The sequential administration of 1 x 10(7) spleen cells, 1 mg of anti-CT-26 I-RNA and 0.4 mg of CT-26 TA resulted in a 20% survival rate of mice bearing established CT-26 tumors. On the other hand, administration of the spleen cells only, I-RNA only or TA only was not effective in inhibiting tumor growth. Similarly, when any one of the three agents (I-RNA, TA and spleen cells) was omitted, no anti-tumor effect was obtained. A higher dose (1 x 10(8)) and a lower dose (1 x 10(6)) of spleen cells decreased the antitumor effect of this combination therapy. A higher dose (2 mg) and a lower dose (0.5 mg) of I-RNA, as well as a higher dose of TA (0.8 mg) had no influence on the antitumor effect. However, a lower dose of TA (0.2 mg) in combination with spleen cells and I-RNA decreased the antitumor effect. When all three agents were administered at higher or lower doses, no antitumor effect was obtained. When mice bearing CT-26 tumors were treated with spleen cells, plus I-RNA directed against a syngeneic but antigenically different tumor (BP/B/5) and BP/B/5 TA, with spleen cells plus CT-26 I-RNA and BP/B/5 TA, or with spleen cells plus BP/B/5 I-RNA and CT-26 TA, no antitumor effect was observed. These results indicate that the antitumor responses observed were due to tumor-specific immune responses. In conclusion, in order to obtain growth retardation or regression of established CT-26 tumor transplants, the sequential administration of all three agents (spleen cells, I-RNA and TA) was required. The optimal doses of each agent were found to be 1 x 10(7) spleen cells, 0.5 mg or 1 mg of I-RNA and 0.4 mg of tumor antigen. Higher or lower doses decreased the antitumor effect. Tumor-specific immune reactions appeared to be involved. (Author abstract) (21 Refs)

39. ANTI-TUMOR EFFECT OF SYNGENEIC SPLEEN CELLS TREATED WITH IMMUNE RNA AND TUMOR ANTIGEN.

Fukushima M, Colmerauer ME, Nayak SK, Koziol JA, Pilch YH
(c/o Pilch), Univ. Hosp.-H891B, 225 Dickinson St., San Diego, CA, 92103
Int J Cancer; 29(1):113-117 1982

The antitumor effect of syngeneic spleen cells, xenogeneic immune RNA (I-RNA) and tumor antigen (TA) was studied in a chemically induced (N-methyl-N-nitrosourethane) colon carcinoma model in BALB/c mice. When the mice were treated, sequentially, with these three elements by local injection under the tumor, complete tumor regression was observed in 25% of the animals. Complete tumor regression was observed in 17% of animals treated by injection of spleen cells pre-incubated with I-RNA in vitro followed by an injection of TA. When spleen cells were treated first with I-RNA and then with mitomycin-C, therapeutic benefit was obtained and the survival rate of mice treated with these spleen cells and TA was significantly higher than that of the control group (no treatment). The antitumor effect of this treatment was abrogated completely when spleen cells were treated with mitomycin-C prior to I-RNA incubation. When spleen cells were incubated with TA in vitro or after incubation with I-RNA and then injected into tumor-bearing mice, no antitumor effect was noted. These data suggest that DNA synthesis and/or lymphocyte proliferation is essential for the action of I-RNA in sensitizing lymphocytes but not essential in the interaction of I-RNA-sensitized lymphocytes with TA. In addition it appeared that, under the conditions used, the participation of host factors was essential in the latter interaction, since treatment of I-RNA-sensitized lymphocytes with TA in vitro was ineffective. (Author abstract) (13 Refs)

40. HIGH-FREQUENCY COTRANSFER OF THE TRANSFORMED PHENOTYPE AND A TUMOR-SPECIFIC TRANSPLANTATION ANTIGEN BY DNA FROM THE 3-METHYLCHOLANTHRENE-INDUCED METH A SARCOMA OF BALB/C MICE.

Hopkins N, Besmer P, DeLeo AB, Law LW
Center Cancer Res., Dept. Biology, Massachusetts Inst. Technology, Cambridge, MA, 02139
Proc Natl Acad Sci USA; 78(12):7555-7559 1981

We transformed BALB/3T3 mouse cells with cellular DNA extracted from the Meth A sarcoma, a 3-methylcholanthrene-induced tumor of BALB/c mice, and asked whether foci arising in the transfection possess the previously defined Meth A tumor-specific transplantation antigen (TSTA). Five of eight foci selected from one experiment possessed Meth A TSTA. DNA extracted from one of the five TSTA-positive clones was used in secondary rounds of transfection transformation. Four out of five foci tested from the secondary transfections possessed Meth A TSTA. These results suggest that in the Meth A sarcoma a transforming gene and a genetic determinant of TSTA are intimately related: they may be identical or very closely linked; alternatively, a particular transforming gene might induce the expression of a particular TSTA. Another possible explanation for these results is that the cotransfer of certain cellular genes by DNA transfection is considerably higher than predicted from the limited studies presently available. (Author abstract) (26 Refs)

41. THE SOLUBLE ANTIGENS OF BALB/C SARCOMA METH-A: A RELATIONSHIP BETWEEN A SEROLOGICALLY DEFINED TUMOR-SPECIFIC SURFACE ANTIGEN (TSSA) AND THE TUMOR-ASSOCIATED TRANSPLANTATION ANTIGEN (TATA).

DuBois GC, Appella E, Law LW, DeLeo AB, Old LJ, Doherty PC, Dement P, Schirrmacher V, Rajan, Klein PA, Lennox ES, Embleton MJ, Martin WJ, Merino F, Truitt RL, Nathenson SG, Bortin MM, Ferrone S
Lab. Cell Biology, NCI, Bethesda, MD, 20205
Transplant Proc; 13(4):1765-1773 1981

Purification of tumor-associated transplantation antigen (TATA) from the methylcholanthrene-induced BALB/c mouse sarcoma (MBMS) Meth-A is reported. MBMS strain CI-4, which possesses a CI-4-specific antigen and does not cross-react with Meth-A or any other tumor, was used as a challenge tumor to determine specificity. Meth-A and CMS-4 strains were used for antiserum absorption studies. Purified plasma membranes from Meth-A cells completely absorbed the cytotoxic activity of anti-Meth-A produced by BALB/c mice immunized with Meth-A cells. Chromatographic analysis showed the Meth-A TATA to be associated with a protein of approx mol wt 60,000-70,000 dalton. Most of the TATA activity was present in a fraction not absorbed on an agarose-hexylamine column. This fraction did not protect mice challenged with CI-4 cells. Fractions not containing TATA activity did not absorb cytotoxic activity. Purified TATA showed an absorption of anti-Meth-A 20-fold greater than that for anti-CMS-4, indicating that TATA has a specificity for Meth-A tumor-specific surface antigen (TSSA). Results suggest that TATA and TSSA are single individual determinants which reside on the same or similar molecules. (16 Refs)

CLINICAL DIAGNOSTIC STUDIES

42. CHEMILUMINESCENCE IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF SOLID TUMOR CANCER PATIENTS.

Braun DP, Harris JE, Maximovich S, Marder R, Lint TF
Dept. Internal Medicine, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Il, 60612
Cancer Immunol Immunother; 12(1):31-37 1981

Blood from patients with advanced malignant disease (14) or minimum residual disease (14) and from healthy adults was heparinized and peripheral blood mononuclear cells (PBMC) measured for chemiluminescence (CL) by scintillation spectrometry. Circulating immune complexes were determined by the Raji cell radioimmunoassay (RIA). Patients with advanced malignant disease had significantly elevated CL in their resting PBMC compared to either healthy persons or patients with minimum residual disease. Stimulation of samples with phorbol myristic acetate elevated CL in samples from both types of cancer patients to much higher peak levels than in those from healthy controls. Vaccination of Stage I lung cancer patients with either Freund's complete adjuvant (FCA) or FCA + extracted tumor-associated antigens (TAA) was followed after 2 mo by elevated PBMC in patients receiving either treatment but not in untreated patients. Serum from lung cancer patients receiving FCA or FCA + TAA caused greatly elevated CL in normal monocytes. Immune complex levels measured by C1q-binding assay did not appear to be correlated with the enhancement effect; Raji-RIA was negative for immune complexes in all treatments. (30 Refs)

43. EFFECT OF DIFFERENT EPSTEIN-BARR VIRUS-DETERMINED ANTIGENS (EBNA, EA, AND VCA) ON THE LEUKOCYTE MIGRATION OF HEALTHY DONORS AND PATIENTS WITH INFECTIOUS MONONUCLEOSIS AND CERTAIN IMMUNODEFICIENCIES.

Szigeti R, Masucci MG, Henle W, Henle G, Purtilo D, Klein G
Dept. Tumor Biology, Karolinska Institutet, S 104 01 Stockholm, Sweden
Clin Immunol Immunopathol; 22(1):128-138 1982

Leukocytes from healthy Epstein-Barr virus (EBV)-seropositive (SP) subjects show significant migration inhibition (LMI) with EBNA (EBV-determined nuclear antigen)-containing extracts derived from nonproducer, EBV-genome-carrying cells, or presented in the form of partially purified EBNA-preparations. Additional EBV antigens, EA and VCA, presented in the form of induced cell extracts do not add any measurable increase to their response. Leukocytes from acute infectious mononucleosis (IM) patients, on the other hand, do not respond to EBNA, but they show a good response to induced EA- or EA and VCA-containing cell extracts. This is in accordance with known differences in EBV-antibody pattern in healthy SPs as contrasted to acute IM patients. Leukocytes from chronic mononucleosis patients resemble those from acute IM patients in their preferential EA/VCA and deficient EBNA response in the LMI test. Cells from four X-linked lymphoproliferative disease (XLP) patients showed complete absence of reactivity to PHA and to EBV antigens in the LMI test, showing a general defect in cell-mediated immune responses. Leukocytes from a group of patients with lymphoproliferative malignancies in remission and elevated EBV-antibody titers showed a variety of responses, resembling normal SP donors, or IM patients, or showing a complete unresponsiveness in the LMI test. (Author abstract) (41 Refs)

44. DETECTION OF PEMPHIGUS-LIKE ANTIGENS ON TUMOR CELL LINES.

Ahmed AR, Murahata R

Div. Dermatology, Univ. California Los Angeles, Sch. Medicine, CHS 52-121, Los Angeles, CA, 90024

Arch Dermatol Res; 271(4):441-445 1981

When sera from eight patients with pemphigus vulgaris were reacted with squamous cell tumor lines, SCaBER and COLO-16, and stained with fluorescein-conjugated anti-human IgG, bright fluorescence was seen, indicating the presence of pemphigus-like antigens on tumor cells. Serum of one of four patients with bullous pemphigoid bound to the cell membranes. Sera from patients with dermatitis herpetiformis or systemic lupus erythematosus did not bind to cells. (16 Refs)

45. PRESENCE OF EPSTEIN-BARR VIRUS DNA IN TONSILLAR TISSUES.

Brichacek B, Suchankova A, Hirsch I, Sibl O, Rezacova D, Zavadova H, Vonka V

Dept. Experimental Virology, Inst. Sera and Vaccines, 101 03 Prague, Czechoslovakia

Acta Virol (Praha); 25(6):361-370 1981

Sera from 48 tonsillar carcinoma (TC) patients, 48 matched controls and 16 recurrent exudative tonsillitis (RET) patients were examined for the presence of Epstein-Barr virus (EBV) associated nuclear antigen (EBNA), early antigen (EA) and virus capsid antigen (VCA). Higher prevalence and significantly higher antibody titers against all three EBV-associated antigens were observed in TC patients in comparison with controls and RET patients. Patients suffering from anaplastic TC had higher titers of antibodies against VCA and EA than TC patients with other histological diagnoses. Five out of 11 TC biopsies obtained from nine patients were positive for EBV DNA at levels of 0.17, 4 to 5, 15 to 18 and in two cases 3 EBV genome equivalents per cellular genome. Among 16 RET patients, 4 were found positive at levels not exceeding 2.17 EBV genome equivalents per cellular genome. Higher titers of antibody against all EBV antigens were found in TC and RET patients with EBV DNA-positive tonsillar tissue than in those with EBV DNA negative tonsillar tissue. (Author abstract) (34 Refs)

46. BLOOD GROUP A AND B ANTIGENS IN SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS.

Si L, Yuan D, Guo S
Dept. Pathologic Anatomy, Xian Medical Coll., Xian, People's Republic of China
Zhonghua Zhongliu Zazhi; 3(2):109 1981

Using an improved specific red cells adhesion test, group A and B antigens were examined in 50 cases of esophageal squamous cell carcinoma with known A and B blood groups. Normal epithelium in tumor specimens from all 50 cases was antigen-positive though antigen activity in each case varied. In contrast, loss of blood group antigens in varying degrees was observed in cancerous tissues from 47 cases, with complete loss in 28 cases and partial loss in 19. The degree of antigen loss was related to the degree of differentiation of tumor tissue. (no Refs) (In CHI)

47. ADJUVANT BCG TUMOUR ANTIGEN FOLLOWING PRIMARY TUMOUR RESECTION: RESULT OF MELBOURNE UNIVERSITY 5 YEAR STUDY (MEETING ABSTRACT).

Steward AM, Clarebrough JK, Wilson A
Departments of Surgery and Cardiothoracic Surgery, University of Melbourne, Melbourne, Australia
Clinical Oncology Society of Australia, November 24-27, 1981, Melbourne, Australia. The Society 70 pp., 1981.

Thirty-four lung cancer patients have been entered by random assignment into a trial of adjuvant therapy using BCG (skin scarification) +/- autologous tumor antigenic preparation (subcutaneous innoculation), following resection of their primary tumor. All treated patients received 3-7 BCG doses at 2-4 weekly intervals, beginning 1 mo following operation. Six also received antigenic tumor preparation by hypertonic KCl fractionation. The treated group consisted of 11 Squamous, 3 Large Cell, 1 Adeno, and 2 Small Cell carcinomas. Controls were 7 Squamous, 6 Large Cell, 2 Giant Cell, 1 Adeno and 1 Small Cell. In the treated group, 7 out of 10 stage I and II are alive and well at 37-62 mo, compared with 2 of 11 controls plus 1 with metastases. Mean survival of those dying in the treated group was 30 mo, compared with 12.8 mo (control). In monitoring patient progress, serial plasma cyclic AMP (c-AMP) levels, serum T3 and thyroid stimulating hormone (TSH) were estimated in 5 patients from each group. Five patients who died within 15 mo, had c-AMP values of 1.1-9.2 Pmol/ml and 4 of these had falling T3 values. Five patients who remained alive and disease free at 16-31 mo had c-AMP values of 0.7-24.8 Pmol/ml, and static or rising T3 levels. Adjuvant therapy given to the treated group prolonged survival, disease free intervals, and appeared to improve quality of life. (no Refs)

48. THE CLINICAL SIGNIFICANCE OF TISSUE POLYPEPTIDE ANTIGEN (TPA) IN THE URINE OF BLADDER CANCER PATIENTS.

Kumar S, Costello CB, Glashan RW, Bjorklund B
Paediatric Oncology Lab., Christie Hosp. and Holt Radium Inst., Manchester M20 9BX, England
Br J Urol; 53(6):578-581 1981

A 2-stage study has been carried out to evaluate the usefulness of urinary tissue polypeptide antigen (TPA) levels in patients with bladder cancer as an adjunct to the routine procedures for detection of bladder tumors. Two-hr urine samples were collected from 83 bladder cancer patients and normal individuals for the first part of the study, 24-hr samples from 54 patients and normal individuals for the second part. Urinary TPA was determined using radioimmunoassay. In 2-hr samples there was no significant difference in the amounts of TPA/I in any of the groups. In contrast, the TPA results of 24-hr urine samples (n = 54) were markedly different from 2-hr samples, and the former correlated very well with the presence or absence of bladder cancer. A reason for this difference may be circadian rhythm effects. (Author abstract) (15 Refs)

49. COMBINED CELL SURFACE ANTIGENS AND CHROMOSOMAL STUDIES IN BLADDER CANCER.

Javadpour N, Roy JB, Bottomley R, Dagg K
Surgery Branch, NCI, Bethesda, MD, 20205
Urology; 19(1):29-32 1982

The conventional histopathologic examination of a primary tumor does not predict the potentiality for invasiveness and recurrence of a superficial low-grade transitional cell carcinoma of the bladder. We have utilized combined cell surface antigens and chromosomal analysis to predict the natural history of the bladder cancer in 20 patients in a double blind study. In this preliminary report it appears that both cell surface antigens and chromosomal abnormalities correlate well with the stages and grades of bladder cancer. (Author abstract) (12 Refs)

50. MULTIPLE MARKER EVALUATION IN HUMAN PROSTATE CANCER WITH THE USE OF TISSUE-SPECIFIC ANTIGENS.

Kuriyama M, Wang MC, Lee CL, Killian CS, Papsidero LD, Inaji H, Loor RM, Lin MF, Nishiura T, Slack NH, Murphy GP, Chu TM
(c/o Chu) Dept. Diagnostic Immunology Res. and Biochemistry, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
JNCI; 68(1):99-105 1982

Serum prostate-specific antigen and prostatic acid phosphatase were simultaneously evaluated in 22 healthy males, 29 patients with benign prostatic hypertrophy, and 192 patients with prostate cancers at various stages as well as in 30 patients with cancers other than prostate cancer. Both markers were quantitated by specific sandwich-type, enzyme-linked, immunosorbent assays with the use of specific antiserum reagents. Serum assays revealed a discordance between these two markers; thus expressions of these two biochemically and immunologically distinct prostate-specific proteins may reflect different aspects in the biology of prostate cancer. A combination test with the use of 7.5 ng of prostate antigen and 15.5 ng of prostatic acid phosphatase/ml of serum, respectively, as cutoff values resulted in a positive detection rate of 58% for prostate cancers of Stages A (7/12) and B (21/36) each, 68% for prostate cancer of Stage C (19/28), 92% for prostate cancer of Stage D (106/116), and only 10% for benign prostatic hypertrophy (3/29). None of 52 other cancers or healthy controls was registered as positive. This study demonstrates that a multiple marker test of tissue-specific antigens can be of an additive value in the immunodiagnosis of cancer and may be a logical and effective approach at this time, in light of the unavailability of human tumor-specific markers. (Author abstract) (22 Refs)

51. THE VALUE OF ESTIMATION OF ABH ANTIGENS IN GYNECOLOGICAL TUMORS.

Tosner J
Gynek.-porop. klinika LF KU, Engelsova 374, 500 06 Hradec Kralove, Czechoslovakia
Cesk Gynekol; 46(9):699-703 1981

Mixed RBC agglutination tests (MEAT) were performed on 124 samples of various tissues from normal and pathological female reproductive tracts to study the ABH isoantigens. Tissue samples included squamous epithelium (SE) from the uterine cervix, cervical glands, the lining of Nabothi's follicles, and the epithelium of the oviducts. Among 17 normal tissues, positive reactions were found in 10 cases, questionable results in 4 cases, and negative results in 3 cases. Among tissues from 12 patients with invasive carcinoma, not one positive result was found, questionable results were found in 9 cases, and negative results in 3 cases. Among 59 SE from patients with abnormal or atypical conditions, carcinoma in situ, or microinvasive carcinoma, positive results were found in 12 cases, questionable results in 42 cases, and negative results in 5 cases. Results indicate that ABH isoantigen tests have no value for differential diagnosis or prognosis of dysplasias of the female reproductive tract. Isoantigens were detected in some cases in the endometrium but not in the corpus luteum. MEAT results had no value for screening or for measuring tumor progression. (18 Refs) (In CZE)

OTHER RELATED STUDIES

52. UTILIZATION OF MONOCLONAL ANTIBODIES IN THE TREATMENT OF LEUKEMIA AND LYMPHOMA.

Ritz J, Schlossman SF
Div. Tumor Immunology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115
Blood; 59(1):1-11 1982

The generation of murine monoclonal antibodies reactive with human leukemia and lymphoma cells has recently led to clinical trials that have begun to evaluate the use of these reagents in the treatment of various leukemias and lymphomas. Several of these studies have demonstrated that infusion of monoclonal antibody can cause the rapid and specific clearance of leukemic cells from the peripheral blood. Intravenously administered antibody also rapidly binds to bone marrow lymphoblasts, and in one instance, has resulted in the partial regression of tumor cell infiltrates in lymph nodes and skin. Unfortunately, clinically significant responses have not in general been achieved, but these clinical studies have identified specific factors that result in the development of resistance to antibody-mediated lysis in vivo. These factors include the presence of circulating antigen, antigenic modulation, reactivity of monoclonal antibody with normal cells, immune response to murine antibody, and the inefficiency of natural immune effector mechanisms. Current research is now being directed towards developing methods to circumvent each of these obstacles. Future clinical studies utilizing antibodies in vitro or with different specificity may demonstrate greater therapeutic efficacy. In addition, monoclonal antibodies can be used as carriers of other cytotoxic agents and in conjunction with other agents that will reduce the total tumor load. Monoclonal antibodies represent new and powerful reagents that may in the near future become an additional therapeutic modality for patients with malignant disease. (Author abstract) (100 Refs)

53. EXPRESSION AND MODULATION OF VIRUS RECEPTORS ON LYMPHOID AND MYELOID CELLS: RELATIONSHIP TO INFECTIVITY.

Morishima T, McClintock PR, Billups LC, Notkins AL
(c/o Notkins) Lab. Oral Medicine, Natl. Inst. Dental Res., NIH, Bethesda, MD, 20205
Virology; 116(2):605-618 1982

Using a sensitive and specific assay for the binding of radiolabeled encephalomyocarditis (EMC) virus to cell surface receptors, we have measured the kinetics of virus attachment to murine lymphoid and myeloid cells, and have shown that receptors for this virus vary with the phase of cell growth and can be modulated or, in some cases, induced. The initial rate constant (KR) for resident peritoneal macrophages was 0.8 X 10(-9) cm3 min-1 cell-1, but after in vivo stimulation the rate of binding increased by a factor of 2. In contrast, unstimulated splenic T and B lymphocytes failed to bind EMC virus, but after exposure to appropriate mitogens, the initial rate constant increased to as high as 6.7 x 10(-9) cm3 min-1 cell-1. Studies with continuous cell lines showed that the binding of virus to receptors varied by up to 10-fold and was greatest during the exponential growth phase as compared to the stationary phase. Although the KR increased following exposure of lymphocytes to mitogens, immunofluorescence revealed that only a small fraction of the cells actually contained viral antigens, suggesting that virus receptors either were induced in only a small subpopulation of lymphocytes or that postattachment restriction prevented viral replication in a large fraction of the cells. A survey of six cloned BALC/c T and B cell lymphomas arrested at different stages of differentiation showed that two of these lymphomas possessed EMC virus receptors, arguing that receptors are present only at certain stages of cell differentiation. Evidence that receptors are functionally important comes from experiments which showed that only cells with a KR greater than 0.1 x 10(-9) cm3 min-1 cell-1 are susceptible to infection. These studies suggest that factors which influence the expression and modulation of virus receptors may determine the outcome of certain viral infections. (36 Refs)

54. HUMAN BLOOD GROUPS M-, N-, T-, AND TN-SPECIFIC SUBSTANCES IN LIPIDIC EXTRACTS OF LINE 10 HEPATOCARCINOMA OF STRAIN 2 GUINEA PIGS.

Springer GF, Cantrell JL, Desai PR, Tegtmeyer H
Immunochemistry Res., Evanston Hosp., Evanston, IL, 60201
Clin Immunol Immunopathol; 22(1):9-19 1982

Live line 10 (L-10) hepatocarcinoma cells of Strain 2 guinea pigs carry immunoreactive human blood group T (Thomsen-Friedenreich)- and Tn-specificities on their surface as determined with human antisera. Disintegrated L-10 cells show in addition M and N activities; this indicates their presence within the tumor cells. Blood groups S and D(Rh0) activities were not demonstrable. M and N but not Tn an T specificities were also found in normal submaxillary and sublingual glands, kidney, and liver of Strain 2 guinea pigs. After extraction of L-10 carcinoma cells with n-butanol-water, all activities resided in the organic phase. Extraction of the organic phase by Sevag's deproteinization procedure yielded nearly eight times as much active material (by wt) in the chloroform layer as in the aqueous layer. Depending on the antisera used, M and N activities of the extracts amounted to 10 to greater than 100% of authentic red cell M and N glycoproteins, Tn activity to approx 75%, and T activity to between 5 and 10% of that of human red blood cell-derived T antigen. The active extracts had less than 0.75% protein and less than 3.50% ash. We report two novel findings: (a) the occurrence of M and N specificities in nonprimates, and (b) the association of these specificities with lipidic substances. (Author abstract) (48 Refs)

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DETECTION/ CHARACTERIZATION/ ISOLATION

1. SELECTIVE BINDING AND COMPLEMENT-MEDIATED LYSIS OF HUMAN HEPATOMA CELLS (PLC/PRF/5) IN CULTURE BY MONOCLONAL ANTIBODIES TO HEPATITIS B SURFACE ANTIGEN.

Shouval D, Wands JR, Zurawski VR, Isselbacher KJ, Shafritz DA
(c/o Shafritz) Dept. Medicine and Cell Biology, Liver Res. Center, Albert Einstein Coll. Medicine, Bronx, NY, 10461
Proc Natl Acad Sci USA; 79(2):650-654 1982

High-affinity 125I-labeled monoclonal antibodies to hepatitis B virus surface antigen (HBsAg) bind to a human hepatocellular carcinoma cell line, PLC/PRF/5, which synthesizes and secretes HBsAg. These monoclonal antibodies of the IgG1, IgG2a, and IgM isotypes are directed against different anti-

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genic determinants on HBsAg and, in the presence of complement, both anti-HBs IgG2a and IgM, but not anti-HBs IgG1, lyse PLC/PFR/5 cells in culture. Although there is a low level of anti-HBs binding (especially with anti-HBs IgM) to human hepatoma cell lines which do not synthesize HBsAg (SK-Hep 1 and Mahlavu cells), this interaction does not lead to complement-mediated cell lysis and is thought to be nonspecific. Minimal binding of 125I-labeled anti-influenza HA antigen IgM binding to PLC/PRF/5 cells was also detected, but this likewise did not lead to complement-mediated cell lysis. These results indicate that a human hepatocellular carcinoma cell line, persistently infected with hepatitis B virus, can be recognized and lysed by monoclonal antibodies directed against specific determinants of HBsAg. Monoclonal antibodies to this viral envelope protein may prove to be useful immunodiagnostic and immunotherapeutic agents when such viral epitopes are expressed on the surface of infected cells. (Author abstract) (33 Refs)

2. MONOCLONAL ANTIBODIES THAT DETECT DIFFERENTIATION SURFACE ANTIGENS ON HUMAN MYELOMONOCYTIC CELLS.

Perussia B, Trinchieri G, Lebman D, Jankiewicz J, Lange B, Rovera G
Wistar Inst., 36th St. at Spruce, Philadelphia, PA, 19104
Blood; 59(2):382-392 1982

We describe here the production and characterization of several new monoclonal antibodies that recognize differentiation antigens present on human cells of the myelomonocytic lineage. The lineage and the stage specificities of our reagents (myeloid-, monocytic-, and myelomonocytic-specific) were determined on the basis of their reactivity with human cell lines and with human peripheral blood and bone marrow cells. Cross-competition experiments demonstrated that some of the antibodies react with the same or closely associated antigenic determinants. Five antigens have been identified in this way: one present on myeloid, one on monocytic, and three on both myeloid and monocytic cells. The possible relationship of our antibodies with other established monoclonal antibodies is discussed, in addition to their use in the in vitro study of the differentiation pathways of human hemopoietic cells and in the characterization of leukemias. (Author abstract) (29 Refs)

3. PROSTATE ANTIGEN: A NEW POTENTIAL MARKER FOR PROSTATIC CANCER.

Wang MC, Papsidero LD, Valenzuela LA, Murphy GP, Chu TM
Dept. Diagnostic Immunology Res., Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Prostate; 2(1):89-96 1981

A prostate-specific antigen (PA) which is distinct from prostatic acid phosphatase (Paph) and has potential diagnostic value is described. Immunoelectrophoresis has demonstrated the presence of PA in prostatic tissues and seminal plasma (0.15-0.45 nanog/g and 0.4-1.8 nanog/g, respectively) and in cultured human prostatic carcinoma cells and spent culture fluid from these cells. Purification of PA from prostatic tissue and seminal plasma is described. PA from prostatic tissue has a mol wt of 33,000-34,000 and an isoelectric point of about 6.9 (one isomer). PA is highly immunogenic and is not immunologically related to Paph. PA was detected in 17/219 patients with advanced prostatic cancer and in none of 20 normal adults, 20 males more than 55 yr old, and 175 nonprostatic cancer patients. PA appears to polymerize or associate with other proteins in the serum and can be released into the circulation from cancerous prostatic tissues. An enzyme-linked immunosorbent assay of PA is described. No PA was found in sera of 17 normal females and 25 female cancer patients; less than 0.1-2.6 nanog/ml was found in 51 normal males. Elevated values of PA were found in 13/19 patients with benign prostatic hyperplasia and in 5/8 patients with prostatic cancer of Stage A, 27/34 of Stage B, 43/56 of Stage C, and 296/344 of Stage D. Elevation of serum PA may be an early warning sign of prostatic abnormality, justifying additional examination procedures. Simultaneous determination of PA and Paph is recommended. (21 Refs)

4. HUMAN PROSTATE SPECIFIC AND SHARED DIFFERENTIATION ANTIGENS DEFINED BY MONOCLONAL ANTIBODIES.

Frankel AE, Rouse RV, Herzenberg LA
Dept. Oncology, Stanford Univ., Palo Alto, CA, 94305
Proc Natl Acad Sci USA; 79(3):903-907 1982

Splenic lymphocytes of BALB/c mice immunized with membrane-enriched fractions of human benign prostatic hyperplasia tissues were fused with the NS-1 light chain-secreting murine myeloma cell line. This generated hybridoma cultures that secreted immunoglobulins reactive in solid-phase radioimmunoassays with membrane preparations of prostatic tissues but not with membrane preparations of apparently normal human liver, spleen, thymus, or erythrocytes. After further screening of immunoglobulin reactivities and cloning of cultures, eight monoclonal antibodies were chosen that demonstrated reactivity with human prostate tissues. These monoclonal antibodies could be placed into at least three major groups - epithelium-specific, polyepithelial, and stroma-specific - on the basis of differential binding to the surfaces of various component cells in the prostate and other epithelia. Two antibodies defined unique protein antigens specific for prostate epithelia that were not crossreactive with prostatic acid phosphatase or the recently described 'prostatic antigen.' These antibodies also detected antigens on malignant prostate tissues as well as other malignant tissues. Four antibodies defined three unique polyepithelial protein antigens (two of the antibodies were different isotypes defining the same protein). Each of the polyepithelial antigens was expressed on a different spectrum of normal epithelial tissues. Two displayed brain tissue crossreactivity, one was present on pancreas, and one was present on platelets. The two antibodies that detected prostatic stromal protein antigens showed different spectra of reactivities. One antibody reacted with apparently all prostatic stromal cells as well as endothelial cells in the prostate and other organs. The other antibody apparently reacted with all prostatic stromal cells as well as myoepithelial and muscle cells in other organs. (Author abstract) (17 Refs)

5. A 53-KILODALTON PROTEIN COMMON TO CHEMICALLY AND VIRALLY TRANSFORMED CELLS SHOWS EXTENSIVE SEQUENCE SIMILARITIES BETWEEN SPECIES.

Jornvall H, Luka J, Klein G, Appella E
Dept. Chemistry I, Karolinska Institutet, S-104 01 Stockholm, Sweden
Proc Natl Acad Sci USA; 79(2):287-291 1982

A heat-stable DNA-binding protein with subunits of about 53 kilodaltons (kDal) was purified from two virally transformed human cell lines (Epstein-Barr virus-positive Raji and Namalwa) and two mouse tumor cell lines (methylcholanthrene-induced Meth A sarcoma and TA3 mammary carcinoma). All four 53-kDal proteins showed closely related total amino acid compositions, similar peptide maps, and identical NH2-terminal amino acid sequences for 20 residues. These 53-kDal proteins are therefore evolutionarily highly conserved, independent of whether they originate from virally or chemically transformed cells. The NH2-terminal sequence and the protein chain as a whole are not hydrophobic; however, some unexpected residue distributions were observed. Comparisons with other proteins reveal no clear sequence similarity with known tumor antigen structures, homologous immunoglobulins, or some other proteins of known sequence. Epstein-Barr virus-determined nuclear antigen also appears to have a different NH2-terminal sequence. Thus, the results show that the 53-kDal proteins represent a unique protein type with little species variation; this finding suggests that these proteins must perform an important common function in different transformation systems. (Author abstract) (38 Refs)

6. DEVELOPMENT OF A MONOCLONAL ANTIBODY AGAINST A TUMOR-ASSOCIATED ANTIGEN.

Peng WW, Bressler JP, Tiffany-Castiglioni E, De Vellis J
Lab. Nuclear Medicine and Radiation Biology, Univ. California, Los Angeles, CA, 90024
Science; 215(4536):1102-1104 1982

A monoclonal antibody-producing hybrid cell line was obtained by fusing mouse myeloma cells with spleen cells from a mouse immunized with C6 glioma cells. This antibody binds to a specific cell-surface antigen that is present on C6 rat glioma cells, transformed astrocytes and oligodendrocytes, and a human glioma cell line but is absent on a normal glial cell line, fibroblasts, and primary cultures of astrocytes and oligodendrocytes. The antigen also appears on tumor tissue of transformed oligodendrocytes but not on normal brain tissue. (Author abstract) (18 Refs)

7. MONOCLONAL ANTIBODIES TO TWO MOUSE BLADDER CARCINOMA ANTIGENS.

Hellstrom I, Rollins N, Settle S, Chapman P, Chapman WH, Hellstrom KE
Program Tumor Immunology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
Int J Cancer; 29(2):175-180 1982

Carcinomas of the urinary bladder of mice were induced by 3-methyl-cholanthrene or FANFT [(4-5-nitro-2-furyl)-2-thioazolyl formamide]. On transplantation in vivo, tumor lines consisting of well-differentiated transitional-cell carcinomas were established. Some tumors were also explanted in vitro. A rat was immunized with a pool of carcinomas and normal bladder tissue and its spleen cells were hybridized with NS-1 mouse myeloma cells. Supernatants of hybrid cells ('hybridomas') were screened for antibody binding to antigens present in bladder carcinomas but not in normal syngeneic urinary bladder, with cell extracts as targets. Hybridomas that appeared to have the required specificity were cloned, tested further against transitional-cell bladder carcinomas, an anaplastic bladder tumor, rhabdomyosarcomas, a mammary carcinoma, myelomas and lymphomas, and normal adult urinary bladder, kidney, lung, spleen, heart, brain, thymus, and whole embryo. Antibody formed by one hybridoma, 2H5, gave significant binding to membranes from five of seven transitional-cell carcinomas but not to membranes from any other tissues. A second hybridoma, IE6, formed antibody to an antigen present in bladder carcinomas and normal liver and, in smaller amounts, in several other normal and neoplastic tissues. Fluorescence microscopy established that both antigens were present at the cell surface of transitional-cell bladder carcinomas. Immunoprecipitation and SDS-polyacrylamide gel electrophoresis were used to identify the target antigens from 125I-labeled cell membrane proteins. The antibody formed by 2H5 was found to identify a protein with a mol wt in the range of 140 kilodaltons, which was detected in transitional-cell bladder carcinoma and, in small amounts, in normal bladder. The molecular nature of the antigen defined by hybridoma IE6 is not known. (Author abstract) (25 Refs)

8. TERATOCARCINOMA ANTIGEN IS SECRETED BY EPIDIDYMAL CELLS AND COUPLED TO MATURING SPERM.

Fox N, Damjanov I, Knowles BB, Solter D
Dept. Pathology, Lab. Medicine, Hahnemann Medical Coll., Philadelphia, PA, 19102
Exp Cell Res; 137(2):485-488 1982

Teratocarcinoma specified antigen SSEA-1, is present on ejaculated sperm, but it is not evident on testicular sperm. We show that SSEA-1 is secreted by the chief cells of the caput epididymis and is then adsorbed to the surface of the spermatozoa during their passage through the epididymis. (Author abstract) (12 Refs)

9. REVERSIBLE AND IRREVERSIBLE STAGES IN THE TRANSITION OF CELL SURFACE MARKER DURI NG THE DIFFERENTIATION OF PLURIPOTENT TERATOCARCINOMA CELL INDUCED WITH RETINOIC ACID.

Ogiso Y, Kume A, Nishimune Y, Matsushiro A
Dept. Microbial Genetics, Res. Inst. Microbial Diseases, Osaka Univ., Yamada-oka 3-1, Suita Osaka 565, Japan
Exp Cell Res; 137(2):365-372 1982

Treatment of a pluripotent teratocarcinoma cell line with retinoic acid (RA) results in the disappearance of peanut agglutinin (PNA) receptors, accompanied with the decrease in F9 antigens and the enhanced secretion of plasminogen activator. However, this type of differentiation was inhibited by feeder cells. Furthermore, the transition of PNA receptor was reversible on the cells treated with RA for 2 days and became irreversible by an additional 2-day treatment with RA. Thus, two stages of teratocarcinoma cell differentiation - reversible and irreversible - were demonstrated. (Author abstract) (22 Refs)

IMMUNOLOGICAL STUDIES

10. A SUBSET OF HUMAN NATURAL KILLER CELLS ISOLATED AND CHARACTERIZED BY MONOCLONAL ANTIBODIES.

Lohmeyer J, Rieber P, Feucht H, Johnson J, Hadam M, Riethmuller G
Medizinische Klinik, Klinikstrasse 36, D-6300 Giessen, W. Germany
Eur J Immunol; 11(12):997-1001 1981

Monoclonal antibodies were induced against leukemic T cells from a patient with chronic lymphocytic leukemia exhibiting natural killer (NK) activity. Two antibodies, termed T811 and M522, reacted by indirect immunofluorescence with distinct subpopulations of normal human mononuclear blood cells. The antibody T811 defines a surface antigen which is restricted to a subset of the T cell lineage. The antigen recognized by the second antibody, M522, is expressed on monocytes and polymorphonuclear leukocytes and, in addition, on 9-17% of nonadherent peripheral blood leukocytes (NAL). It is shown that the total NK activity of NAL is confined to the subset of cells expressing the M522-defined antigen. Moreover, the portion of NK cytotoxicity associated with T lymphocytes is mediated by a subpopulation which is characterized by the simultaneous expression of the T811-and the M522-defined antigens. This population comprises about 4% of NAL and could be isolated to a purity of greater than 85%. (Author abstract) (20 Refs)

11. TUMOR PRODUCTION IN THE NUDE MOUSE, FIBRINOLYTIC ACTIVITY AND CROSS-REACTIVITY WITH ANTIMELANOMA SERA OF VARIOUS HUMAN TUMOR CELL LINES.

Bruggen J, Fogh J, Sorg C
Dept. Experimental Dermatology, Univ. Munster, Von-Esmerch-Str. 56, D-4400 Munster, W. Germany
J Cancer Res Clin Oncol; 102(2):141-152 1981

It has been reported previously that antisera produced in non human primates against many cultured human melanoma lines recognize tumor-associated antigens on the melanoma cells. The reactivity correlated with other parameters of malignancy, such as rapidity of tumor growth in nude mice an d release of plasminogen activator. In this study we have investigated whether these antisera also react with non melanoma cancer lines and searched for a correlation between this reaction and the other parameters of malignancy. There was cross-reactivity of the 10 sera with 4-43% of the 46 non melanoma lines compared to 62-100% of the 16 melanoma lines, indicating a preferential reactivity with melanoma lines. For the non melanoma lines no correlation was found between the release of plasminogen activator, the degree of tumorigenicity in the nude mouse or the reactivity of surface antigens as detected with anti-melanoma sera. (Author abstract) (45 Refs)

12. MONOCLONAL ANTIBODIES TO THE HUMAN MAMMARY GLAND. I. DISTRIBUTION OF DETERMINANTS IN NON-NEOPLASTIC MAMMARY AND EXTRA MAMMARY TISSUES.

Foster CS, Edwards PA, Dinsdale EA, Neville AM
Ludwig Inst. Cancer Res., Royal Marsden Hosp., Sutton, Surrey SM2 GPX, England
Virchows Arch [Pathol Anat]; 394(3):279-293 1982

Mouse monoclonal antibodies have been raised to the human milk fat globule membrane. The distribution of the antigens detected by four of the antibodies has been examined in formalin-fixed, paraffin-embedded human tissues by light microscopic immunocytochemistry. The four antibodies stain lactating breast and normal resting breast. Two exclusively stain the luminal membranes of breast epithelial cells. A third antibody stains in addition the lateral membranes of duct epithelial cells. The fourth antibody stains both epithelial and myoepithelial cells. None of the antibodies is breast specific, nor do they stain every epithelial cell within the breast. Instead, each antibody reveals a complex and heterogeneous distribution of staining throughout the normal tissues. Within the breast, the staining by a given antibody is usually segmental and conforms to secretory units and their associated ducts. Similarly heterogeneous patterns of staining are also observed in the extramammary normal tissues. Despite the apparent morphological identity between breast epithelial cells when examined by conventional light microscopy, the hitherto unrecognized 'functional' heterogeneity, which as been revealed by the monoclonal antibodies could have importance in understanding the biology of the normal breast and the pathology of breast cancer. (Author abstract) (18 Refs)

13. MONOCLONAL ANTIBODIES TO THE HUMAN MAMMARY GLAND. II. DISTRIBUTION OF DETERMINANTS IN BREAST CARCINOMAS.

Foster CS, Dinsdale EA, Edwards PA, Neville AM
Ludwig Inst. Cancer Res., Royal Marsden Hosp., Sutton, Surrey SM2 5PX, England
Virchows Arch [Pathol Anat]; 394(3):295-305 1982

A range of primary and metastatic human breast carcinomas has been examined with respect to the staining by four monoclonal antibodies which were raised to the human milk fat globule membr ane. Within the normal breast the luminal epithelial cells expressing the antigens detected by the monoclonal antibodies were heterogeneous in their distribution. The heterogeneity was not only confined to single cells, but also to regions within the breast. The breast carcinomas also expressed the antigens in a variable manner. Morphological differentiation and functional differentiation, defined by the monoclonal antibodies, were not invariably coincident. Lymph node metastases gave similar results to the primary carcinomas. The monoclonal antibodies have revealed a heterogeneity, with respect to surface antigenic expression, within the normal and neoplastic breast epithelium. This cellular heterogeneity of breast carcinomas, may have significant prognostic and therapeutic implications in the management of primary breast cancer. (Author abstract) (17 Refs)

14. IMMUNOLOGIC ASPECTS OF THE PROSTATE.

Lubaroff DM, Reynolds CW, Canfield L, McElligott D, Feldbush T
Dept. Urology, Univ. Iowa, Iowa City, IA, 52242
Prostate; 2(3):233-248 1981

Present knowledge of tumor immunology is reviewed, and recent research results using the Dunning R3327 tumor of the Copenhagen rat as an immunologic model of prostatic adenocarcinoma and continuing work, are described. The R3327 tumor, a well-differentiated adenocarcinoma which will grow into the sc space of the flank or within the prostate is described, and its histological appearance is shown. Earlier results included cryodestruction of the primary R3327 tumor by trocar probe procedure and demonstration of tumor-specific antigens and production of immune responses to them in xenogeneic, allogeneic, and syngeneic immunizations. Cell-mediated responses have been successfully demonstrated, including a nonspecific or natural killer activity in lymph nodes, spleen, and peripheral blood. Cryosurgery + BCG have been demonstrated to induce a tumor-protective immune response in the R3327 system. Problems associated with immunotherapy are reviewed, and studies demonstrating reduced immunocompetence in patients with prostatic cancer or benign prostatic disease compared to normal individuals are described. (26 Refs)

15. SCINTIGRAPHY AND DISTRIBUTION OF LABELED ANTIBODIES IN RATS WITH TUMORS.

Sharp JG, Osborne JW, Cheng HF, Coop KL, Zimmerman GR
Radiation Res. Lab., Univ. Iowa, Iowa City, IA, 52242
Eur J Nucl Med; 7(1):28-34 1982

Experiments with in vivo localization of iv injected radiolabeled tumor antibodies (Ab) in Holtzman rats with an x-ray-induced mucoid adenocarcinoma of the intestine are described. Tumor antigen was induced in New Zealand white rabbits using tissue from several animals, and the rabbit serum globulins were separated by electrophoresis and labeled with 131I. Globulins receiving final electrophoretic and diffusion separation were called 'purified'; others were 'unpurified.' The distribution of 131I-labeled unpurified and purified Ab, 131I-labeled non-tumor-specific gamma globulin, and 131I-labeled serum albumin were studied in normal and tumor-bearing rats. Scanning was accomplished by rectilinear camera and gamma camera; tissue distribution of labeled material was determined by scintillation spectrometry of digested tissue samples. Comparison of scans revealed tumors greater than 2.0 g in mice receiving all three radio-labeled agents, but none showed tumors dependably when the tumors were less than 1.0 g. Localization of 131I-labeled Ab was variable, and useful levels of Ab were present in only a few cases. The presence of circulating tumor antigens capable of binding the Ab is responsible for much of the variability. (31 Refs)

16. MODIFICATION OF AGE-RELATED IMMUNE DECLINE IN MICE DIETARILY RESTRICTED FROM OR AFTER MIDADULTHOOD.

Weindruch R, Gottesman SR, Walford RL
Dept. Pathology, Sch. Medicine, Univ. California, Los Angeles, CA, 90024
Proc Natl Acad Sci USA; 79(3):898-902 1982

Although weaning-initiated dietary restriction of rodents is known to increase max survivorship and inhibit spontaneous late-life disease and immunologic aging, restriction begun in adulthood has been much less thoroughly evaluated. In the present studies, male mice of a long-lived F1 hybrid strain were gradually restricted dietarily beginning at 12 mo or older until their body wt stabilized at 60-70% of controls. Underfeeding decreased the number of nucleated cells per spleen but increased the percentage of T cells. For mice restricted at 12, 17, or 22 mo and tested at various ages thereafter, the [3H]thymidine uptake of spleen cells after phytohemagglutinin stimulation significantly exceeded values for age-matched unrestricted controls. Restriction did not, however, alter either splenocyte responses to concanavalin A or to B-cell mitogens or phytohemagglutinin responses of peripheral lymph node cells. In the splenic plaque-forming cell response to injected sheep erythrocytes, restricted and control mice differed more clearly in response kinetics than in peak levels. The splenic cell-mediated lymphocytotoxic response to alloantigens was comparable in old mice (27-29 mo) restricted since 12 mo of age with that of young (5-to 6-mo) controls and was greater than that of age-matched old controls. Spontaneous tumors were observed less frequently in 19-to 25-mo-old mice restricted at 12 mo of age than in mice restricted at 17 mo or in controls. Our results indicate that appropriate food restriction initiated in adulthood influences immunosenescence and spontaneous tumor incidence in a fashion not unlike its weaning-initiated counterpart. (Author abstract) (31 Refs)

17. HUMORAL FACTORS INVOLVED IN THE MECHANISM OF REACTIVITY OF THE MICROPLATE LEUKOCYTE ADHERENCE INHIBITION ASSAY.

Russo AJ, Howell JH, Goldrosen MH
Dept. Surgical Oncology, Tumor Immunology Group, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Immunol Commun; 10(7):611-630 1981

To study if specific antigen(s)-induced adherence inhibition is due to direct cell contact or mediated by a soluble factor, spleen cells and enriched populations of B-cells and T-cells from normal C57Bl/6J mice and mice bearing progressively growing MCA-38 tumors were incubated with MCA-38 tumor antigen(s) and control B-16 melanoma antigen(s) for 1 hr at 37 C. The supernatants of these cultures were harvested and evaluated for their ability to induce adherence inhibition of normal peritoneal cells. Supernatants of MCA-38 sensitized B-cells but not T-cells could induce adherence inhibition of normal peritoneal cells. Furthermore, supernatants of MCA-38 sensitized spleen cells could not induce adherence inhibition of normal peritoneal cells, despite the fact that these cells can directly undergo specific antigen(s)-induced adherence inhibition. However, the sensitized spleen cells, after removal of the supernatant, were less adherent than comparable cells incubated with media alone, suggesting that the reactive cell within the spleen cell population adsorbed the soluble mediator as it was being generated. Affinity chromatography studies revealed that the biologically active soluble mediator contained IgG. Gel filtration studies indicated that the soluble mediator had a mol wt greater than 190,000 daltons. Thus, in this murine tumor model, leukocyte adherence inhibition is dependent upon the interaction between sensitized B-cells and specific tumor antigen(s) to produce a soluble mediator and is an antibody-mediated phenomenon. (Author abstract) (19 Refs)

18. TUMOR-ASSOCIATED SURFACE MEMBRANE ANTIGENS ON CFUS: CHARACTERIZATION USING THE FLUORESCENT ACTIVATED CELL SORTER.

Hasthorpe S, Rogerson J
Cancer Inst., 481 Little Lonsdale St., Melbourne, 3000, Australia
Exp Hematol; 10(1):9-19 1982

Antiserum raised in rabbits against the FMP1.1 mouse tumor cell line is known to cross-react with GM-CFC and BFUE from normal marrow using the complement-dependent cytoxicity assay. It has been found that this antiserum is cytotoxic to CFUs, either with or without complement addition in vitro. Immunofluorescent analysis using the fluorescent activated cell sorter (FACS) has confirmed this immunological cross-reactivity with CFUs. Recovery of antibody-coated CFUs posed a potential problem in FACS experiments due to in vivo destruction by either opsinization or cytotoxic lysis. Experiments involving enzyme digestion (papain) of antibody and preincubation of bone marrow cells to allow antibody capping did not show improved recovery of CFUs. However, incubation of anti-FMP1.1 coated bone marrow cells with specific anti-rabbit IgG serum resulted in up to 67% of CFUs being detected. Dual parameter sorting with FACS, involving forward light scatter and fluorescence, gave about 26 and 19 times enrichment of GM-CFC and BFUE, respectively, whereas CFUs were enriched by only six times. These colony-forming cells were found in the cell population with high intensity forward light scatter and with relatively low fluorescence. Bone marrow cells undergoing regeneration 7 days after 5-fluorouracil (5-FU) treatment of mice exhibited more intense immunofluorescence than normal marrow cells. In particular, a distinct population of lymphocytes in 5-U treated marrow reacted with anti-FMP1.1 serum, which was not observed with normal marrow. (Author abstract) (27 Refs)

VIRUS ASSOCIATED ANTIGENS

19. HEPATITIS B ANTIGEN IN THE LIVER IN HEPATOCELLULAR CARCINOMA IN SHIKOKU, JAPAN.

Akagi G, Furuya K, Otsuka H
2nd Dept. Pathology, Sch. Medicine, Kuramoto-cho 3-18-15, Tokushima 770, Japan
Cancer; 49(4):678-682 1982

An analysis of 105 autopsy cases (77 male, 28 female) of hepatocellular carcinoma (HCC) showed that 90 cases (85.7%) were associated with liver cirrhosis, of which 75 cases (83.3%) were of the macronodular type. Hepatitis B surface antigen (HBsAg) was detected with orcein stain in the hepatic tissue in 58 cases (55.2%). The incidence of HBsAg in cases of HCC patients with cirrhosis (58.9%) was higher, but not significantly, than that in those without cirrhosis (33.3%). The mean age of HBsAg-positive cases was 5 yr less than that of HBsAg-negative cases, the age distributions therefore being significantly different. (Author abstract) (43 Refs)

20. THE EFFECT OF CHRONIC HABITUAL ALCOHOL INTAKE ON THE DEVELOPMENT OF LIVER CIRRHOSIS AND HEPATOCELLULAR CARCINOMA: RELATION TO HEPATITIS B SURFACE ANTIGEN CARRIAGE.

Ohnishi K, Iida S, Iwama S, Goto N, Nomura F, Takashi M, Mishima A, Kono K, Kimura K, Musha H, Kotota K, Okuda K
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Cancer; 49(4):672-677 1982

To study the effects of habitual alcohol intake on the latency period for the development of liver cirrhosis and hepatocellular carcinoma (HCC), 158 patients with cirrhosis and 79 with HCC were analyzed with respect to age at the time of diagnosis. They were classified into four groups based on hepatitis B surface antigen (HBsAg) in serum, and the history of intake of more than one small bottle of Japanese 'sake' or an equivalent per day for more than 10 yr. The av age of HBsAg positive male cirrhotics with a drinking habit (n = 10) was 38.8 yr, 10.5 yr younger than that of those without a drinking habit (n = 8) (p less than 0.05). The av age of HBsAg negative cirrhotics with a drinking habit (n = 97) was 47.9 yr, 8 yr younger than that of those not drinking (n = 36) (p less than 0.001). There was no significant difference in the laboratory data between these groups. The av age of the HBsAg positive HCC patients with a drinking habit (n = 20) was 48.9 yr, 9 yr younger than that of those without a drinking habit (n = 12) (p less than 0.05). The av age of HBsAg negative male HCC cases with habitual intake of more than 126 ml of ethanol per day was 51.0 yr (n = 8), 10 yr younger than that of nondrinking male HCC cases (n = 11) (p less than 0.05). These data suggest that habitual alcohol intake may promote the development of liver cirrhosis and HCC, especially in HBsAg carriers. (Author abstract) (29 Refs)

21. AFLATOXINS, B1, B2, G1, G2 IN PRIMARY LIVER CELL CARCINOMA.

Onyemelukwe GC, Ogbadu GH, Salifu A
Dept. Medicine, Ahmadu Bellow Univ., Zaria, Nigeria
Toxicol Lett; 10(2):309-312 1982

The presence or absence of circulating aflatoxins and other mycotoxins in adults (25-65 yr old) with primary liver cell carcinoma (PLCC) was investigated. Serum and urine samples were obtained from each of 20 and 7 PLCC patients, respectively. Serum aflatoxin levels were determined by Velasco Fluorotoxin meter. Mean serum aflatoxin, B1, B2, G1, and G2 levels were 0.069, 0.095, 0.083, and 0.040 ug/ml, respectively. Aflatoxin B1 levels greater than 0.15 ug/ml were measured in three patients; however, higher aflatoxin levels may have been present due to 24 hr serum clearance values of 0.025 to 0.050 ug/ml in these subjects. Hepatitis B surface antigen was detected in eight patients. Two other fungal metabolites, zearalenone, associated with cervical cancer in mice, and Phoma sorghina metabolite, associated with hemorrhagic thrombocytopenia, were identified in two separate urine specimens. Although evidence of aflatoxin carcinogenicity in man is inconclusive, foodstuffs should be protected from excessive aflatoxin contamination. (14 Refs)

22. AFLATOXIN LEVELS IN SERA OF HEALTHY FIRST TIME RURAL BLOOD DONORS: PRELIMINARY REPORT.

Onyemelukwe GC, Ogbadu G
Dept. Medicine, Ahmadu Bello Univ. Hosp., Zaria, Nigeria
Trans R Soc Trop Med Hyg; 75(6):780-782 1981

Serum levels of aflatoxin B1 (AB1), aflatoxin B2 (AB2), aflatoxin G1 (AG1), and aflatoxin G2 (AG2) were assayed in 20 first-time blood donors (25-40 yr old) and 15 sick persons (controls). The blood donors were all farmers from rural villages of the Guinea Savannah of Nigeria, cultivating and living on local staple foods (millet, sorghum, rice, and yams). The controls (including a man with nasopharyngeal carcinoma and a woman with hydatidiform mole) lived in villages near the hospital. Mean serum aflatoxin (AFL) levels in the blood donors were 0.123, 0.118, and 0.118 ug/ml for AB1, AB2, and AG1, respectively, and 0.064 ug/ml for AG2. Four blood donors showed AB1 levels of 0.2 ug/ml. Hepatitis B surface antigen (H BS-Ag) was present in the serum of 1/20 blood donors, who showed a low serum AFL level and no clinical disease. In the control group, serum AFL levels were significantly lower than in the farmers. The highest AFL levels (0.14 ug/ml of AB1, 0.24 ug/ml of AB2) were observed in the patient with nasopharyngeal cancer. Three patients with liver cirrhosis were positive for HBS-Ag and showed low serum AFL levels. Since liver function tests were normal in the farmers and in the absence of histological examination of their livers, it was difficult to speculate whether any of them had entered the multistage process of hepatic carcinogenesis. Further research is needed to evaluate the interactions (if any) between AFL and Epstein-Barr, hepatitis B, and cytomegaloviruses. (16 Refs)

23. EFFECTS OF N-BUTYRATE ON EPSTEIN-BARR VIRUS-CARRYING LYMPHOMA LINES.

Anisimova E, Saemundsen AK, Roubal J, Vonka V, Klein G
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J Gen Virol; 58(part1):163-171 1982

The compound n-butyrate has been shown to induce Epstein-Barr virus (EBV) antigen synthesis in certain EBV-carrying lymphoma lines. We have studied the effect of n-butyrate on two EBV-positive Burkitt lymphoma lines by immunofluorescence and electron microscopy. In the producer line P3HR-1, the drug induced not only early antigen (EA) and virus capsid antigen (VCA) synthesis, as shown before, but also increased the number of cells containing virus particles. The transition from VCA expression to the formation of virus particles was much more effective in treated cells than in EBV antigen-producing cells of the same line. The productive cycle was associated with the development of characteristic morphological changes. In the non-producer Raji cells, n-butyrate induced EA in only a minor fraction of the cells. There were, however, clear signs of differentiation in the direction of plasma cells. Two days after the addition of n-butyrate 80% of the Raji cells could be classified as plasmablasts. After 72 hr, 20% of the cells appeared as typical plasma cells. (Author abstract) (33 Refs)

24. INDUCTION OF EPSTEIN-BARR VIRUS NUCLEAR ANTIGEN AND DNA SYNTHESIS IN A HUMAN EPITHELIAL CELL LINE AFTER EPSTEIN-BARR VIRUS INFECTION.

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Dept. Hematology, Hadassah Univ. Hosp., Jerusalem, Israel
J Virol; 41(2):703-708 1982

The association of Epstein-Barr virus (EBV) with nasopharyngeal carcinoma is supported by the presence of EBV genomes in the epithelial elements of the tumor and by elevated antibody titers to EBV-specific antigens in the patients; the levels of these titers are related to the clinical course of the disease. However, since most laboratory data suggest that EBV is a B-lymphotropic virus, it is unclear how the virus becomes associated with the epithelial elements of the nasopharynx. The purpose of the present work was to find a human model system to study this association. A human epithelial line (U) was found that could be directly infected by EBV, and viral functions, the induction of EBV nuclear antigen and cellular DNA synthesis, were demonstrated. The U line was established in 1957 by the late H J Van Kooten (Kok-Doorschodt at the University of Utrecht), and although it is no longer diploid, it exhibits density inhibition. When U cells were infected with EBV, EBV nuclear antigen was expressed in 6 to 16% of the cells, 1 and 2 days after infection with B95-8 virus, but not with the P3HR-1 strain. No evidence for virus replication was obtained; immunofluorescence staining for early antigens and virus capsid antigens gave negative results. Quantitative adsorption experiments for EBV indicated that the adsorption capacity of U cells is significant (60% of Raji cells). The present results also demonstrated that infection with the virus overcomes block(s) in cellular DNA synthesis caused by 5-fluorodeoxyuridine. The induction of DNA synthesis was determined by increased incorporation of [3H]thymidine into the cells. The highest level of isotope incorporation was observed at about 15 hr after infection and thereafter decreased. Analysis of the induced DNA indicated that it was of cellular origin. (Author abstract) (36 Refs)

25. B LYMPHOBLAST ANTIGEN (BB-1) EXPRESSED ON EPSTEIN-BARR VIRUS-ACTIVATED B CELL BLASTS, B LYMPHOBLASTOID CELL LINES, AND BURKITT'S LYMPHOMAS.

Yokochi T, Holly RD, Clark EA
(c/o Clark) Regional Primate Res. Center and Dept. Genetics, Univ. Washington, Seattle, WA, 98195
J Immunol; 128(2):823-827 1982

Two new cell surface antigens expressed on B lymphoblastoid cell lines (B-LCL) were defined with cytotoxic mouse monoclonal antibodies. One marker, BB-1 (for B lymphoblast antigen-1), was detected on human and nonhuman primate B-LCL, Epstein-Barr virus (EBV)-activated B cell blasts, most Burkitt's lymphomas, and Ia+ B lymphoblast-like myelomas. Polyclonal B cell activators such as pokeweed mitogen (PWM) and lipopolysaccharide (LPS) also induced the expression of BB-1 on immunoglobulin (Ig)-positive cells.In contrast, BB-1 could not be detected on normal lymphoid tissues by complement-dependent cytotoxicity and immunofluorescence (IF) assays or by analysis with a fluorescence-activated cell sorter (FACS). T cell blasts, T cell leukemias, and pre-B cell or erythroblastic leukemia cell lines were also BB-1 negative. Of particular interest was the finding that BB-1 was expressed on the Jijoye lymphoma but only marginally on a subline of Jijoye, P3HR-1, that lacks receptors for EBV and produces a defective virus incapable of transforming lymphocytes. A second lymphoblast antigen (LB-1) unlike BB-1, was present on both T and B cell blasts and virus-transformed T- and B-LCL but not on normal lymphoid tissues. (Author abstract) (50 Refs)

26. IMPROVED IMMUNOFLUORESCENCE ANTIGENS FOR DETECTION OF IMMUNOGLOBULIN M ANTIBODIES TO EPSTEIN-BARR VIRAL CAPSID ANTIGEN AND ANTIBODIES TO EPSTEIN-BARR VIRUS NUCLEAR ANTIGEN.

Gallo D, Walen KH, Riggs JL
Viral and Rickettsial Disease Lab., California Dept. Health Services, Berkley, CA, 94704
J Clin Microbiol; 15(2):243-248 1982

Epstein-Barr viral capsid antigen (VCA) and nuclear antigen produced by modified procedures were evaluated for use in measuring VCA IgM and Epstein-Barr virus (EBV) nuclear antigen antibody responses in sera from patients with EBV infection. VCA production was stimulated with a phorbol ester, and the EBV nuclear antigen (EBNA) cells were fixed in suspensions to eliminate loss of antigen during the drying process. Approx 70% of the tumor-promoter agent-stimulated P3HR-1 cells fluoresced when reacted with VCA-IgM- or VCA-IgG-positive sera. In the anticomplement immunofluorescence test for EBNA antibody, 100% of the cells (except the dead ones) in every smear tested showed dense nuclear fluorescence with positive sera. The improved antigen preparations were evaluated in tests on 122 sera. Twenty patients possessed antibody patterns consistent with recent EBV infection. Fifteen patients showed VCA-IgM antibody and no antibody to EBNA; both IgM and EBNA antibodies were present in later specimens taken form five patients. Patients examined in the study were heterophil negative and all were diagnostic problem cases. Patients presenting with lymphatic disease who are heterophil negative and for whom other infections have been ruled out are diagnostic problems for the clinician, especially when lymphoma is a possibility. Reliable serological tests for EBV should be helpful for studying these problem cases. (18 Refs)

27. NASOPHARYNGEAL CARCINOMA IN AMERICAN CHILDREN: EPSTEIN-BARR VIRUS-SPECIFIC ANTIBODY TITERS AND PROGNOSIS.

Naegele RF, Champion J, Murphy S, Henle G, Henle W
Div. Infectious Diseases, St. Jude Children's Res. Hosp., Memphis, TN
Int J Cancer; 29(2):209-212 1982

Seven American juvenile patients with undifferentiated or nonkeratinizing nasopharyngeal carcinoma (NPC) were examined serially for Epstein-Barr virus (EBV)-specific antibody spectra and titers in sera. At diagnosis, all showed antibody patterns characteristic of NPC: ie, high titers of IgG antibodies to viral capsid antigen (VCA) and to the diffuse (D) component of the early antigen complex. Six patients had IgA antibodies to VCA, and four to the D component. In the patients who responded to therapy with complete and maintained remissions, the IgG antibodies to D and the IgA antibodies to VCA and D decreased to undetectable levels within 12 to 30 mo. By contrast, of the four patients who responded only transiently to therapy, three showed substantial increases and one continuously high titers of IgG anti-D and IgA anti-VCA. The increases in antibody titers preceded clinical recognition of recurrent tumors by 1 to 6 mo. Three of these patients have died and the fourth is alive with disease. These data indicate that American juvenile NPC does not differ from the adult disease observed anywhere in the world. They reaffirm the potential usefulness of EBV-specific serology in the diagnosis and prognosis of NPC and the monitoring of patients following therapy. (Author abstract) (35 Refs)

28. ISOLATION OF AN ANTIGEN FOR DIAGNOSIS OF ENZOOTIC CATTLE LEUKEMIA USING AGAR GEL IMMUNODIFFUSION TECHNIC.

Mateva V
Central Res. Veterinary Inst., Sofia, Bulgaria
Vet Med Nauki; 18(4):45-46 1981

A method of isolation of cattle leukemia virus antigen is described. The virus was isolated from the culture medium or from the cells of fetal lamb kidney infected with cattle leukemia virus. The antigen formed a precipitation band with the leukemic sera. Activity and specificity of precipitation band did not differ from that produced by glucoprotein antigens. The antigen was effectively used for the diagnosis of enzootic cattle leukemia. (no Refs) (In BUL)

29. CONTRIBUTION TO EPIDEMIOLOGIC STUDIES OF BOVINE ENZOOTIC LEUKOSIS.

de Alencar RA, Rodrigues FM, Vianna WO
Instituto Biologico, Sao Paulo, Brazil
Biologico; 47(9):249-253 1981

An epidemiologic study of bovine enzootic leukosis (BLV) was performed, using cohabitation (CO), feeding (FE), or blood transfusion (BT). The BT experiment consisted of transferring 200 ml of blood from two serologically positive animals into two that were serologically negative. Immunodiffusion tests (IDT), performed on days 30, 60, 90, 120, and 180, using antigen Leukassay-B, all gave negative results. Eleven cows that were clinically negative for bovine leukemia virus (BLV) showed positive results with the IDT for blood, three showed positive results for colostrum 24 hr after delivery, and five for colostrum 48 hr after delivery. Blood of three of their heifers gave positive results 24 hr after birth and five gave positive results 48 hr after birth; 6 mo later none of the heifers gave positive results. The CO and FE of serologically positive or negative heifers for BLV and of cows that were serologically positive but clinically negative, did not endanger the heifers. Cross reaction was not observed between serum containing antibodies for BLV and serum containing antibodies for bovine diarrhea virus. (5 Refs) (In POR)

30. MALIGNANT TRANSFORMATION OF CELLS OF NEWBORN HAMSTERS BY HERPES SIMPLEX VIRUS TYPE 2.

Kitsak VIa
Central Inst. Advanced Training for Physicians, Moscow, USSR
Vopr Virusol; (6):750-753 1981

Malignant transformation induced by herpes simplex virus Type 2 (HSV-2) was studied in cultured fibroblasts from 3-5 day old hamsters. Infection of primary culture with UV-inactivated HSV-2 caused morphological transformation of cells; first signs of morphological transformation were detected 14-25 days after infection. Characteristic features of morphological transformation were the loss of contact inhibition, multilayer growth, and progressive replacement of epithelioid cells by fibroblastlike cells. Immunofluorescent analysis showed the presence of virus-specific antigen in 5-30% of transformed cells, but transformed cells did not produce the infectious virus. Syngeneic newborn hamsters inoculated sc with transformed cells developed fibrosarcomas. Duration of the latent period was correlated with the number of passages in vitro (from 12 wk after 27 passages to 4 wk after 50 passages). (11 Refs) (In RUS)

31. MAMMARY TUMOR VIRUS (MTV) ANTIGEN EXPRESSION IN MALE GENITAL ORGANS FROM VARIOUS INBRED STRAINS OF MICE.

Imai S, Morimoto J, Tsubura Y
Second Dept. Pathology, Nara Medical Univ., Nara, Japan
Nara Igaku Zasshi; 32(5):570-573 1981

In an effort to demonstrate the route of extrachromosomal male transmission of MTV, MTV antigen expression in the epididymis and coagulating glands of the male genitalia of various strains of inbred mice was investigated with the aid of microimmunodiffusion (micro-ID) test. The MTV expression was studied in the following strains of mice: high mammary cancer strains (GR, DD/Tbr, SHN, SLN, C3H/HeA), intermediate mammary cancer strains (DDD and KF), and low mammary cancer strains with low and moderate incidence of leukosis (but including AKR/RU). In the mice with positive micro-ID tests, the frequency of MTV antigen expression was generally lower in the epididymis than in the coagulating gland. The frequency of MTV antigen expression also depended on the mouse strains; high mammary cancer strains showed more frequent antigen expression in the male genital organs than low mammary cancer strains showed. Overall, there was no marked difference with regard to the frequency of antigen expression among the high mammary cancer strains. These findings confirmed that the male genitalia play an important role in paternal transmission of MTV. (17 Refs)

32. ADENOVIRUS TYPE 12 T ANTIGEN-RELATED SURFACE ANTIGEN DETECTED BY IMMUNOFLUORESCENCE ON THE MEMBRANE OF TRANSFORMED AND INFECTED CELLS.

Vasconcelos-Costa J, Ribeiro G
Unit Virology, Gulbenkian Inst. Science, Apartado 14, P-2781 Oeiras Codex, Portugal
Virology; 117(1):135-145 1982

THA cells, derived from a hamster tumor induced by adenovirus type 12 (Ad12), were analyzed by immunofluorescence for the presence of virus-specific surface antigens. S antigen is a surface antigen detected on suspended living cells by a serum collected from hamsters immunized with Ad12. Besides S antigen, a new surface antigen (surface-T) was observed in formaldehyde-fixed cells treated with anti-T serum. Anti-T serum is not reactive against S antigen in living cells and anti-S serum did not detect surface-T antigen. The membrane location of surface-T antigen was confirmed with a Staphylococcus aureus binding assay. Surface-T antigen seems specific for Ad12, as it is not observed in hamster embryo cells, and is not recognized by antisera against SV40-or polyoma-T antigens nor by antiserum against hamster embryonic antigens. Surface-T antigen is also seen in infected KB cells but not in abortively infected RK13 cells. Anti-P serum, raised against an extract of infected

RK13 cells, failed to detect surface-T antigen. Experiments with adsorbed anti-T and anti-S sera confirmed the specificity of surface-T antigen and its distinctiveness from S antigen. (Author abstract) (22 Refs)

33. SPECIFIC INTERACTION OF THE SV40 T ANTIGEN-CELLULAR P53 PROTEIN COMPLEX WITH SV40 DNA.

Reich NC, Levine AJ
(c/o Levine) Dept. Microbiology, State Univ. New York Stony Brook, Sch. Medicine, Stony Brook, NY, 11794
Virology; 117(1):286-290 1982

Three forms of the simian virus 40 (SV40) large tumor antigen (T antigen), free T antigen from infected monkey cells, T antigen-p53 complex from virus-infected mouse cells, and T antigen-p53 complex from SV40-transformed mouse cells, were examined for their abilities to bind specifically to SV40 DNA. Employing an immunoassay that detected T antigen and/or p53 protein bound to restriction fragments of viral DNA, it was shown that all three of these forms of SV40 T antigen bind preferentially to the restriction fragment of SV40 DNA containing the nucleotide sequence at the origin of viral DNA replication. Free p53 protein alone failed to bind to SV40 DNA in this assay. These results indicate that the SV40 T antigen-p53 protein complex displays the same SV40 DNA binding specificity as free T antigen obtained from a productive infection. (Author abstract) (24 Refs)

TUMOR ASSOCIATED TRANSPLANTATION ANTIGENS

34. STUDIES OF THE MECHANISMS FOR THE INDUCTION OF IN VIVO TUMOR IMMUNITY. VI. INDUCTION OF SPECIFIC AND NONSPECIFIC CELL-MEDIATED IMMUNITY IN TUMOR-BEARING HOSTS AND ITS CORRELATION WITH TRANSPLANTATION TUMOR IMMUNITY.

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Cell Immunol; 66(1):45-58 1982

Studies were performed to determine the development of cell-mediated cytotoxic response at tumor site in C57BL/6 mice bearing progressively growing FBL-3 ascites leukemia. The effectors isolated from tumor ascites are found to be highly cytotoxic for leukemic target cells. The levels of cytotoxicity obtained with effectors isolated from tumor site are generally higher than those obtained with immune mice. This cytotoxicity is both specific and nonspecific. The specific cytotoxicity against tumor-associated antigen is mainly mediated by T cells and the nonspecific cytotoxicity against unrelated tumor cells is mediated largely by macrophages. The T-cell-enriched preparation did not given significant natural killer activity. When testing the ability of these effectors to produce in vivo immunity against the challenge of FBL-3, it was found that only T cells could confer the transplantation-type immunity, but the immunity was transient. The macrophage-enriched preparation isolated from tumor ascites failed to give in vivo protection. These findings indicate that in FBL-3 system, mice with progressively growing tumor are able to develop immune response against tumor cells. However, this immunity is probably interfered with by a suppressor factor(s) or suppressor cells which restrict their activity to eliminate the tumor cells effectively. (Author abstract) (36 Refs)

35. TUMOR BEARER T CELLS SUPPRESS BCG-POTENTIATED ANTITUMOR RESPONSES. I. REQUIREMENTS FOR THEIR EFFECT.

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Cellular Immunobiology Section, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Cell Immunol; 66(1):121-138 1982

Mice bearing established syngeneic tumors fail to reject them when immunized according to protocols based on optimal conditions for BCG potentiation of specific delayed-type hypersensitivity (DTH) and antitumor immunity. Serum factors from mice bearing either the poorly immunogenic mastocytoma, P815 (MA), or the more antigenic sarcoma, Meth A, have been shown to depress both DTH and antitumor immunity. This report demonstrates that lymphoid cells adoptively transferred from these tumor-bearing hosts also can suppress the efferent and afferent phases of DTH to tumor-specific antigens in both BCG-primed and unprimed syngeneic hosts. Suppressor cells (SC) were detected in spleen, thymus, and lymph nodes draining the tumor site, but not in distant superficial lymph nodes. Maximal suppressor activity appeared 6 days after tumor implantation and wanted by 18 days. Suppression of the afferent phase of both the BCG-primed and unprimed responses was antigen specific; suppression of the efferent phase of the BCG-primed response was also specific but SC could partially suppress the unprimed responses to sheep red blood cells (SRBC). Amputation of 6-day-old tumors resulted in the disappearance of splenic SC within 2 days but did not affect SC in draining lymph nodes. SC suppressed DTH in a dose-dependent manner but even the highest doses tested did not totally eliminate the response. Depression of the peak DTH reaction was not accompanied by significant abrogation of antitumor activity. If, however, SC were transferred during the ongoing antitumor response, immunity was partially suppressed. Efferent-phase SC were sensitive to treatment with anti-Thy 1 sera and complement but were unaffected by B-cell depletion. (Author abstract) (29 Refs)

36. IN SITU IMMUNOLOGIC CHARACTERIZATION OF CELLULAR CONSTITUENTS IN LYMPH NODES AND SPLEENS INVOLVED BY HODGKIN'S DISEASE.

Poppema S, Bhan AK, Reinherz EL, Posner MR, Schlossman SF
(c/o Bhan) Dept. Pathology, Massachusetts General Hosp., Boston, MA, 02114
Blood; 59(2):226-232 1982

The cellular constituents in lymph nodes and spleens of patients with Hodgkin's disease were studied with a series of monoclonal antibodies directed against human thymocyte, peripheral T-cell, and Ia antigens. Utilizing both an immunoperoxidase technique on frozen tissue sections and indirect immunofluorescence on cell suspensions, we found that a majority of lymphocytes were T cells, since they stained with anti-T1 and anti-T3 antibodies, which react with all peripheral T cells. In addition, most of these cells were reactive with anti-T4 antibody, which defines the helper/inducer T-cell population, whereas only a minority of cells stained with anti-T5 and anti-T8 antibodies, which are reactive with suppressor/cytotoxic T cells. Moreover, a large proportion of T cells expressed T10 antigen, which is found on activated T cells. A minority of the T cells also expressed Ia antigen(s), again suggesting that some of the T cells are activated. In contrast, the Reed-Sternberg cells did not react with any of these anti-T-cell antibodies or with anti-IgM antiserum, but displayed strong membrane and cytoplasmic staining with anti-Ia antibody. Taken together, these findings suggest that Reed-Sternberg cells are not of T-cell lineage but may be derived from antigen-presenting reticulum cells in the thymus-dependent areas of lymphoid tissues; these cells are normally associated with T4+ cells. (Author abstract) (40 Refs)

37. MECHANISMS OF SYNGENEIC TUMOR REJECTION; SUSCEPTIBILITY OF HOST-SELECTED PROGRESSOR VARIANTS TO VARIOUS IMMUNOLOGICAL EFFECTOR CELLS.

Urban JL, Burton RC, Holland JM, Kripke ML, Schreiber H
La-Rabida Univ., Chicago Inst., Univ. Chicago, Chicago, IL, 60649
J Exp Med; 155(2):557-573 1982

Several progressively growing variants of the UV-induced 1591 regressor fibrosarcoma are described and studies on changes in susceptibility of the variants to natural killer cells and to tumor-specific or cross-reactive T cell-mediated immunity are reported. Five to 10-wk-old female C3H/HeN mice from a colony of germ-free-derived animals and normal nude animals were used. Five of 1591 regressor fibrosarcoma were isolated from normal animals to determine the selective pressures that had been exerted upon the parental tumor by normal immunocompetent hosts. The variant tumor cell lines could neither induce nor be killed by tumor-specific lymphocytes, suggesting that selection had been exerted against tumor cells expressing the tumor-specific antigen. No selection against natural killer cell activity or against nonspecific T cell-mediated immunity appeared to occur because progressor tumor cells were highly sensitive to these types of effector cells and induced these effector cells more effectively than did the parental tumor. Nude mice were capable of generating natural killer activity in response to a challenge with progressor tumor cells, but were unable to mount a nonspecific T lymphocyte response. Progressor tumors grew at a significantly faster rate in nude animals than in normal mice. Tumor nonspecific T cell-mediated immunity may play a role in retarding tumor growth, but the absolute resistance of normal animals to progressive tumor growth critically depends upon the presence of T cell-mediated tumor-specific immunity. Neither NK cells nor nonspecific cytotoxic T lymphocytes appear to play a role in immunoselection against this tumor in normal immunocompetent hosts. (34 Refs)

38. HIGH-FREQUENCY GENERATION OF NEW IMMUNORESISTANT TUMOR VARIANTS DURING METASTASIS OF A CLONED MURINE TUMOR LINE (ESB).

Bosslet K, Schirrmacher V
Behringwerke, 3550 Marburg, W.Germany
Int J Cancer; 29(2):195-202 1982

A metastatic variant of a chemically induced lymphoma (ESb) from a DBA/2 mouse was found to activate in syngeneic hosts specific anti-tumor cytolytic T lymphocytes (CTL) which recognized on the tumor a distinct tumor-associated antigen. Upon metastasis of a cloned ESb tumor line from a sc site to the spleen, the tumor cells which were originally sensitive to lysis by anti-ESb CTL became specifically immunoresistant. The development of immunoresistant variants after tumor-cell transplantation followed a defined kinetic and organ pattern: they were first detected in the spleen, then also in the liver and in the late stage of tumor progression they were the predominant tumor type in all involved organs. No immunoresistant tumor variants were generated in immunoincompetent animals such as nude (nu/nu) mice. Immunoresistant variants also developed when immunosensitive ESb clones were inoculated into animals specifically preimmunized against ESb. In fact, these variants were the only type of cells eventually growing out from such animals causing death from metastasis in spite of the specific immune status of the host. The change of tumor antigen expression described here differs from antibody-induced antigenic modulation in that it is genetically transmitted and stable in tissue culture. The immunoresistant tumor variants which did not preexist in the starting, twice-cloned cell population represent a new type of immune escape variant. (Author abstract) (24 Refs)

39. DETECTION OF TYPE-SPECIFIC ANTIGENIC DETERMINANTS OF MURINE MAMMARY TUMOR VIRUSES WITH CELL-MEDIATED IMMUNE ASSAYS.

Lopez DM, Sigel MM, Schlom J
Univ. Miami, Miami, FL, 33101
Proc Soc Exp Biol Med; 169(1):144-148 1982

Cell-mediated immune assays were used to detect type differences among mouse mammary tumor viruses (MMTV) obtained from various mouse strains. The diversity of MMTVs found and their recognition by the lymphoid cells may explain variations in mouse mammary tumor development and differences in their metastatic potential. (23 Refs)

40. THE BINDING AFFINITY OF POLYOMA-TUMOR SPECIFIC ANTIGEN (TSTA) TO RECEPTORS OF LYMPHOCYTE POPULATIONS.

Ochalek T, Porwit-Bobr Z, Radzioch D
Dept. Microbiology and Immunology, Inst. Molecular Biology, Jagiellonian Univ., Krakow, Grodzka 53, Poland
Folia Histochem Cytochem (Krakow); 19(4):189-196 1981

The incorporation of 3H-thymidine was used as a means to determine the stimulation of thymus and lymph node cell populations by TSTA obtained and purified from the surface of polyoma cells in a conditioned medium with T cell growth factor. The specificity of TSTA was demonstrated after the immunization of CBA mice in adoptive transfer of lymph node cells followed by challenge with polyoma cells. The binding affinity of TSTA to receptors of lymph node cells and thymocytes from CBA mice was tested by radiolabeling. Differences in binding affinity estimated on the basis of equilibrium constant (K) and maximal binding capacity (n) were found between thymus and lymph node cell populations but not between lymph node cell populations themselves. The lack of change in the binding affinity of 125I-TSTA to receptors of lymph node cells in various experimental mice was also discussed. (Author abstract) (20 Refs)

41. KINETICS OF THE IMMUNE RESPONSE OF TUMOR-BEARING HAMSTERS TO TWO SIMIAN VIRUS 40 CODED NON-STRUCTURAL POLYPEPTIDES PRESENT IN SIMIAN VIRUS 40 TUMOR CELLS.

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Int J Cancer; 29(2):217-222 1982

The kinetics of the immune response of hamsters transplanted with virus-free SV40 tumor cells (TSV5) to two SV40-coded non-structural proteins of 94,000 daltons (T antigen) and 17,000 daltons (T antigen) was studied in order to determine if the variation in the immune reactivity of serum from tumor-bearing animals towards these proteins can be explained on the basis of differential immune response during various stages of tumor growth. The results demonstrate that individual animals vary in their capacity to respond immunologically to T and t antigens in SV40-transformed cells and that, further, the immune response to T and t antigens is influenced by the stage of tumor development. (Author abstract) (31 Refs)

42. BIOLOGY OF SIMIAN VIRUS 40 (SV40) TRANSPLANTATION ANTIGEN (TRAG). VIII. RETENTION OF SV40 TRAG SITES ON PURIFIED SV40 LARGE T ANTIGEN FOLLOWING DENATURATION WITH SODIUM DODECYL SULFATE .

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Virology; 117(1):267-270 1982

Simian virus 40 (SV40) large tumor (T) antigen was isolated from SV40-infected permissive and -transformed cells by immunoprecipitation with anti-T sera and purified by electrophoresis on solubilizable SDS-polyacrylamide gels. This method proved to be a rapid and efficient procedure for purifying T antigen as 74% of the immunoprecipitated T antigen was subsequently recovered The purified, SDS-denatured large T antigen retained its ability to react with anti-T antibody and to immunize mice against a challenge of syngeneic SV40 tumor cells, indicating that the antigenic sites present on the large T antigen molecule that induce a tumor rejection response in vivo are resistant to denaturation by SDS. (Author abstract) (25 Refs)

43. CELL SURFACE BINDING AFFINITY OF SIMIAN VIRUS 40 T-ANTIGEN.

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Virology; 117(1):173-185 1982

Simian virus 40-transformed cells are characterized by a virus-induced tumor transplantation antigen (SV40 TSTA) defined in vivo by the rejection of tumorigenic SV40-transformed cells in SV40-immunized mice and in vitro by SV40 tumor cell-specific cytotoxic T cells. Several experimental findings support the notion that SV40-infected and -transformed cells express SV40 large tumor antigen (T-Ag) or closely related antigens on the cell surface (surface T). In this report, evidence is presented for a cell surface binding affinity of SV40 T-Ag solubilized and extracted by disruption of SV40-transformed and SV40-infected cells in growth medium. Incubation of various transformed and nontransformed living monolayer cells in situ with these extracts led to a significant uptake of T-Ag to the cell surface (called 'externally bound T-Ag') up to 2-5x higher amounts in comparison to native surface T on SV40-transformed cells. This was demonstrated by the highly sensitive 125I-protein A assay using rabbit antisera directed against purified SV40 T-Ag. Serological analysis of T-Ag in cellular extracts and of externally bound T-Ag revealed no apparent differences suggesting the cell surface binding affinity as a new property of SV40 T-Ag. We interpret our results as an indication that this property enables purified T-Ag to initiate the cellular immune response necessary for the SV40-tumor rejection in mice. (Author abstract) (40 Refs)

CLINICAL DIAGNOSTIC STUDIES

44. PLASMA IMMUNOABSORPTION ALTERATION OF HUMORAL IMMUNE COMPONENTS AS A TREATMENT FOR CANCER.

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Cancer Bull; 33(6):278-281 1981

Plasma immunoabsorption as a method for altering humoral response to restore cytolytic function of the immune system is discussed. Tumor-bearing hosts develop increased titers of antitumor antibodies capable of inducing in vivo tumor cell lysis; however, serologic molecules (including IgG subclasses 1, 2, and 3, antiglobulins, circulating tumor antigens, and circulating antibody-antibody complexes) block the humoral response and tumor growth continues. Plasma immunoabsorption can reverse the blocking activity, presumably by complement-mediated tumor cell lysis. The procedure involves separation of plasma from cellular components and absorption of immunoreactive substances from an equilibrium system. The important element of such a system is the absorbent on the column or filter, which must interact with components of the humoral immune system. Animal studies and a clinical trial using a staphylococcal paste layered over a millipore filter resulted in definite antitumor response. Purified protein A bound to solid-phase supports is a newer and safer absorbent, and preliminary studies among breast cancer patients have documented antitumor effects and decreased toxic side effects compared with the staphylococcal system. (27 Refs)

45. ABNORMAL ANTI-EPSTEIN BARR VIRUS ANTIBODIES IN CARRIERS OF THE X-LINKED LYMPHOPROLIFERATIVE SYNDROME AND IN FEMALES AT RISK.

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J Immunol; 128(2):904-907 1982

The asymptomatic hemizygous female carriers of the x-linked lymphoproliferative syndrome (XLP) have abnormal antibody responses to EBV. This suggests partial expression of the defect that leads to EBV-provoked life-threatening diseases in their affected sons. EBV specific antibodies were measured in 65 serum samples of 12 obligate carrier females and 7 of their daughters (females at risk) during periods ranging from 1 to 5 yr. Abnormal qualitative antiviral capsid antigen (VCA) IgG titers were nearly fourfold higher than normal controls, two carriers had persistent IgM anti-VCA antibody, two-thirds had persistent IgA anti-VCA antibody, and half of the women had titers to early antigen (EA). Five of seven females exhibited a similar persistent pattern. In contrast, none of the unaffected family members nor 23 normal controls expressed IgA or IgM titers to VCA even with high exposure to the virus, and anti-EA was detected in only one control. Therefore, these findings may prove useful for detecting carriers of the syndrome. Abnormal anti-EBV titers similar to the carrier pattern have been reported in patients and other immunosuppressed individuals, and are indicative of active viral infection. (Author abstract) (31 Refs)

46. CLINICAL EVALUATION OF NCA IN PATIENTS WITH CHRONIC MYELOCYTIC LEUKEMIA.

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Int J Cancer; 29(2):133-137 1982

NCA, a normal colon and granulocyte antigen, which has been found in large amounts in myelocytes and metamyelocytes and in smaller amounts in neutrophil granulocytes, was studied in 50 CML patients in various stages of the disease. Radioimmunoassay was used to demonstrate NCA in serum. Untreated CML patients had a mean level of 732 ug NCA/l, poorly controlled patients 421 ug/l and well-controlled patients 160 u/l. These values differ significantly from the mean of healthy persons, which was 71 ug NCA/l. The serum NCA levels were related to the number of maturing myeloid cells in blood, and to the clinical course in the chronic phase of CML. In blast crisis low values with a mean of 109 ug NCA/l was found. Patients with ANLL had a low mean level, 50 ug/l. Low levels of NCA could not be attributed to antibodies to NCA. NCA is a normal myeloid differentiation antigen. Despite this, its occurrence in serum in leukemic patients differs from normal. This probably has to do with the abnormal amount as well as the release of NCA by leukemic maturing myeloid cells. (Author abstract) (27 Refs)

47. DETERMINATION OF ULTRASTRUCTURAL PEROXIDASES AND IMMUNOLOGIC MEMBRANE MARKERS IN THE DIAGNOSIS OF ACUTE LEUKEMIAS.

Marie JP, Perrot JY, Boucheix C, Zittoun J, Matyre MC, Kayibanda M, Rosenfeld C, Mishal Z, Zittoun R

Service d'Hematologie, Hotel Dieu, 1 place du Parvis Notre Dame, 75181 Paris Cedex 04, France

Blood; 59(2):270-276 1982

Detection of membrane markers and ultrastructural peroxidase activity was carried out on the blasts of 16 apparently nonmyeloid adult acute leukemias. These patients were selected from 73 adult leukemic patients by the negativity of their routine cytochemical myeloid markers: ie, myeloperoxidase, cholesterase activity, and Sudan Black B staining. B and T acute lymphoid leukemias (ALL) were excluded from the study. After concurrent testing for human T lymphocyte antigen (HuTLA), common ALL antigen (cALL), Ia-like antigens, and peroxidase activity at the electron microscopic level (POEM), only two patients remained undifferentiated (cALL-, POEM-). Two other cases were classified as following: six common ALL (cALL+, POEM-), one pre-T-ALL (cALL+, HuTLA+, POEM-), five very poorly differentiated acute myelogenous leukemia (AML) (cALL-, POEM+), and two mixed leukemias (cALL+, POEM+). Terminal deoxynucleotidyl transferase activity (TdT) was measured in seven cases and was found to be present at high levels in four cases of cALL and in the two cases of acute undifferentiated leukemias (AUL); it was absent in two cases of AML. Cytogenetic analysis had showed that 2 of the cALLs, three of the AMLs, and the two mixed leukemias were Ph1+. We conclude that POEM detection is useful in apparently nonmyeloid leukemias with negative immunologic lymphoid markers, and that the existence of a Ph+ chromosome should be investigated, particularly in the unusual case of mixed (lymphoid-myeloid) acute leukemia. (Author abstract) (24 Refs)

48. INHIBITION OF LEUKOCYTE MIGRATION BY HUMAN THYROID ADENOCARCINOMA ASSOCIATED ANTIGENS.

Aoki N, DeGroot LJ

Dept. Medicine, Kinki Univ. Sch. Medicine, Sayama-cho, Minamikawachi-gun, Osaka, Japan

Acta Endocrinol (Copenh); 99(1):56-63 1982

The agarose microdroplet leukocyte migration inhibition (LMI) assay was used successfully to demonstrate the existence of cell-mediated immunity to tumor-associated antigens (TAA) in patients with thyroid adenocarcinoma. With the use of crude tumor extracts obtained from a mixed papillary-follicular adenocarcinoma of the thyroid by hypertonic KCl solubilization, 50.0% positive reactivity was observed in metastatic thyroid cancer patients, whereas no healthy donors or patients with auto-immune thyroid disease showed a positive response in the LMI assay. Among responders, no antigenic cross-reactivity was found between the crude tumor extracts and non-cancerous antigens such as human thyroglobulin, or extracts of Graves' disease thyroid tissue, or kidney tissue. The crude tumor extracts were fractionated by Sephadex G-200 chromatography and the effluent materials were pooled into three fractions. The high mol wt fraction corresponding to the side of thyroglobulin elution, and the intermediate mol wt fraction, showed no TAA activity. The low mol wt fraction including substances of molecular size near that of ovalbumin (45,000 mol wt) selectively retained the TAA activity. TAA activity in the low mol wt fraction was concentrated in comparison to the crude tumor extracts. When this fraction was tested in the LMI assay, positive reactivity increased in metastatic thyroid cancer patients, but no response was observed in either healthy donors or patients with thyroid auto-immune diseases. The LMI response to TAA was more striking in patients with active metastatic cancer than in those whose metastatic foci had responded to treatment. (Author abstract) (24 Refs)

49. ECTOPIC PRODUCTION OF PLACENTA-'SPECIFIC' TISSUE PROTEINS (PP5 AND PP11) BY MALIGNANT BREAST TUMORS.

Inaba N, Renk T, Daume E, Bohn H

(c/o Bohn) Res. Laboratories, Behringwerke AG, Postfach 1140, D-3550 Marburg (Lahn), W. Germany

Arch Gynecol; 231(1):87-90 1981

An enzyme-bridge immunoperoxidase technique was used to demonstrate the production of two placenta-'specific' tissue proteins, PP5 and PP11 in sections of the breast cancers of 16 patients. The specific antisera against human PP5 and PP11 were raised by immunizing rabbits with the purified antigens. An IgG fraction of goat antiserum against rabbit immunoglobulin was used as the second antibody. Peroxidase-rabbit antiperoxidase (PAP) complex was then applied. A slightly modified Mason PAP method was used to demonstrate the tissue antigens. Clear positive staining for PP5 was observed in 10/16 (62.5%) breast cancers, and for PP11 in 7/15 (46.7%). Positive staining was only observed in the cytoplasm. All of the specimens positive for PP11 were also positive for PP5; all six specimens negative for PP5 were also negative for PP11. Positive staining was more frequent in cells found in the periphery of the cancer mass than those in the center. No staining was observed in apparently normal breast tissues and histiocytes in the tissues and/or in the vessels. These determinations in sera might be of use in screening for breast cancer and for monitoring therapy or detecting metastases in patients with established disease. (17 Refs)

50. LEUKOCYTE MIGRATION INHIBITION ASSAY IN PATIENTS WITH PROSTATE ADENOCARCINOMA.

Wright GL, Schellhammer PF, Reid JW, Seig SM, Faulconer RJ, Brassil DN
Dept. Microbiology and Immunology, Eastern Virginia Medical Sch., P.O. Box 1980, Norfolk, VA, 23501
Prostate; 2(2):121-131 1981

The leukocyte migration inhibition (LMI) assay was used to measure cell-mediated immunity (CMI) responses in 44 patients (56-92 yr old) with prostate cancer as a measurement of putative tumor antigens in 3 M KCl extracts of fresh tumor tissue. Six patients had Stage A disease, 12 Stage B, 11 Stage C, and 15 Stage D. Controls included 13 patients with transitional cell carcinoma of the bladder, 18 with renal cell carcinoma, 14 with breast carcinoma, 4 with colon carcinoma, 4 with lung carcinoma, 19 with benign prostate hyperplasia, and 30 normal volunteers. Using a prostate tumor extract, LMI was found in 27/44 (61%) of patients with prostate tumors, 7/19 (37%) with benign prostatic hyperplasia, 26% of patients with nonprostatic cancers, and 10% of normal donors. Control extracts obtained from normal prostate tissue, benign prostate hyperplasia tissue, and tissues from other tumors had statistically less LMI reactivity when reacted against WBC from patients with prostatic tumors. LMI reactivity of prostate cancer patients did not correlate with the clinical state of disease, although there was less reactivity with advanced disease. (21 Refs)

51. CELL SURFACE ANTIGEN - A STUDY IN BLADDER TUMOURS.

Kulkarni JN, Kamat MR, Gangal SG, Talwalkar GV
G.U. Service, Tata Memorial Hosp., Bombay, India
J Surg Oncol; 19(1):14-17 1982

Thirty bladder tumors of various stages and grades were examined for the presence of ABO (H) cell surface antigen using specific red cell adherence (SCRA) technique. Ten patients with Stage A disease and low grade tumor (Grade I) retained the antigens, whereas all patients with high stage disease (B,C,D) and high grade tumors showed absence of antigen. When these data were correlated with recurrence pattern and metastasis or invasion rate, patients who did not show the antigen at the initial visit developed metastases and had poor prognoses. The patient who had expressed the antigen by positive SCRA had fewer recurrences and a longer tumor-free interval. Hence if SCRA is done in all bladder tumors at the initial visit and at subsequent follow-up, it can be used as a biological marker. (Author abstract) (7 Refs)

52. BLOOD GROUP ABO (H) CELL SURFACE ANTIGENS IN BLADDER TUMORS INVADING THE CHORION. THE PROGNOSTIC VALUE OF THEIR DETERMINATION BY IMMUNOFLUORESCENCE. A RETROSPECTIVE STUDY OF 125 CASES.

Vacant J, Le Portz B, Augustin I, Hammou JC, Fella C, Delignieres S, Maiolini R, Masseyeff R, Abelanet R, Steg A
GRET, G.I.E. FAX, 5, rue Eugene Emmanuel, 06000 Nice, France
Ann Urol (Paris); 16(1):24-29 1982

In a group of 125 patients with Stage A bladder tumors, antigens of the AB and H blood group were collected and studied. All patients were studied after a follow-up of at least 5 yr. In 18 patients there was no recurrence. In 20 patients, there was Stage A recurrence, and in 76 patients there was at least Stage B recurrence. In 11 cases, the condition was uncertain. In the group of 11 patients whose tumor cells were immunofluorescent positive, all were alive at 5 yr follow up and all except one were free of all tumors. In the group of 37 patients who had a positive but heterogeneous immunofluorescence, 14 patients (37.8%) were alive at 5 yr follow up and 23 had died. Of 77 patients whose cells all tested negative, 20 patients (27%) were alive at 5 yr and 8 of these had no recurrence. It is suggested that homogeneous retention of the surface antigens is a favorable prognostic indicator even if the tumor has already infiltrated the chorion. Although the disappearance of surface antigens had been proven to be adverse, the significance has not yet been established. (27 Refs) (In FRE)

53. A STUDY OF THE DISTRIBUTION OF ABH CELL SURFACE ANTIGENS IN BLADDER TUMORS BY INDIRECT IMMUNOFLUORESCENCE.

Vallancien G, Rouger P, Leclerc JP, Kuss R
Clinique Urologique, Hopital de La Pitie, 83, boulevard de l'Hopital, 75634 Paris, France
Ann Urol (Paris); 16(1):30-33 1982

In a study of 30 patients with bladder tumors (transitional cell epitheliomas), only three cases (10%) retained A, B, or H antigens on the urothelium. In a control group of 30 patients with healthy bladders, antigens were present in all cases. Four types of distribution of A, B, and H antigens were found. There was no correlation between tumor stage or grade and the type of immunofluorescent distribution. Absence of fluorescence of the tumor epithelium was found in 10/17 of the Grade I tumors. None of these tumors enolved toward muscle infiltration. In 4/5 cases of Grade II or III tumors, there was absence of fluorescence, and invasion or infiltration of the muscle occurred. Of 18 histologically, superficial tumors which invaded only the mucous membrane, four lost antigens and evolved toward muscle infiltration. Two tumors which were positive recurred in the same superficial stage. In the other cases, the tumor lost all or part of its antigenicity and evolved toward the infiltration of muscle. Infiltration of the muscle occurred in 3/8 Stage I tumors which were completely negative. The other five lost part of their antigens, but none evolved to muscle infiltration. Although the loss of ABH antigens did not seem to be associated with tumor grade or stage, the persistence of the ABH antigens was considered a favorable prognostic factor. (17 Refs) (In FRE)

54. THE USE OF IMMUNOFLUORESCENCE FOR IDENTIFYING ABH CELL SURFACE ANTIGENS IN FROZEN BLADDER SECTIONS.

Devonec M, Blanc-Brunat N, Bouvier R, Muchada E, Dubernard JM
Service d'Urologie, Pavillon v, hopital Edouard Herriot, place d'Arsonval, Lyons, France
Ann Urol (Paris); 16(1):34-39 1982

The results of an immunofluorescent study of 24 patients with initial or recurrent bladder tumors were compared with six controls having normal mucous membranes. All of the controls presented the same characteristics with homogeneous fluorescence limited by the basal membrane. The fluorescence was limited to membranes and did not include the cytoplasm. Antigenic expression was always completely loss in carcinoma in situ. Papillary lesions also lost antigenic expression. In certain hyperplastic states, fluorescence disappears from the basal to the more superficial layers. In carcinoma in situ and papillary lesions the fluorescence was limited to the basal membrane. When histological examinations were correlated with fluorescent results, the transition between healthy epithelium and the mucosa of carcinoma in situ or papillary lesions could be determined by a loss of normal antigenic expression as fluorescence diminished in the areas of the tumors. Since microscopic interpretation was considered too subjective a method of interpretation, flow cytometry is recommended as the most appropriate tool for fluorescent study. (14 Refs) (In FRE)

55. IMMUNOFLUORESCENCE AS A MEANS OF IDENTIFYING ABH CELL SURFACE ANTIGENS IN UROTHELIAL CELLS FROM BLADDER IRRIGATION FLUID.

Devonec M, Fontaniere B, Blanc-Brunat N, Muchada E, Sarkissian J, Dubernard JM
Service d'Urologie, Pavillon V, Hopital Edouard Herriot, place d'Arsonval, 69374 Lyon, France
Ann Urol (Paris); 16(1):40-43 1982

The results of an immunofluorescent study of 24 patients with initial or recurrent bladder tumors were compared with six controls having normal mucous membranes. In the control group basal cells and intermediary cells from bladder irrigations displayed intense fluorescence. The superficial cells in the washings displayed either little or no fluorescence. In washings from cancer patients, leukocytes and evidence of bleeding in numerous urothelial cells revealed associated hemorrhagic conditions or infections. The loss of antigenic expression (AE) appeared directly related to the neoplastic character of certain cells. The normal cells from the washings were used as reference cells and defined the degree of normal AE. Surrounding neoplastic cells lost all AE in their membranes. The fluorescence which they presented was a nonspecific, autofluorescence of the cytoplasm. Since the loss of AE occurs in aging cells, the interpretation AE for diagnostic purposes in bladder cancer is recommended only insofar as certain conditions are met. These conditions include an estimate of cell viability and a precise measurement of the normal membrane fluorescence. (7 Refs) (In FRE)

56. THE USE OF THE RED CELL SURFACE ANTIGEN TO PREDICT THE MALIGNANT POTENTIAL OF TRANSITIONAL CELL CARCINOMA OF THE URETER AND RENAL PELVIS.

Hall L, Faddoul A, Saberi A, Edson M
Dept. Urology and Pathology, Washington Hosp. Center, Washington, DC
J Urol; 127(1):23-25 1982

This is the first report on the use of the red cell surface antigen test in predicting the malignant potential of transitional cell carcinoma of the ureter and renal pelvis. In 29 cases evaluated there was an 80% correlation. The red cell surface antigen determination was shown to have practical value in the management of these tumors. (Author abstract) (10 Refs)

OTHER RELATED STUDIES

57. IMMUNO-HISTOLOGICAL ANALYSIS OF BONE MARROW INVOLVEMENT IN LYMPHOPROLIFERATIVE DISORDERS.

Pizzolo G, Chilosi M, Cetto GL, Fiore-Donati L, Janossy G
Sezione di Enatologia, Policlinico di Borgo Roma, 37134 Verona VR, Italy
Br J Haematol; 50(1):95-100 1982

Cryostat sections from bone marrow biopsies submerged in gum-sucrose solution and snap-frozen can be stained with various antisera to detect both the membrane and cytoplasmic antigens on normal and malignant populations in their tissue environments. This technique seems to be the method of choice to analyze the degree of BM involvement in cases of non-Hodgkin's lymphoma where conventional histology provides equivocal results. The uniform expression of only one type of light chain in B lymphoma and the analysis of the T cell infiltrate in T-CLL using monoclonal antibodies is demonstrated. (Author abstract) (9 Refs)

58. THE IMMUNOLOGY OF CANCER OF THE HEAD AND NECK WITH PARTICULAR REFERENCE TO ORAL CANCER.

Scully C
Univ. Dept. Oral Medicine and Pathology, Immunology Unit, Glasgow Dental Hosp., 378 Sauchiehall St., Glasgow G2 3JZ, Scotland
Oral Surg; 53(2):157-169 1982

Interest in the possible influence of immunologic mechanisms on the development of cancer of the head and neck has increased over the past decade. This review discusses the evidence for the influence of the immune response on the development of cancer, the immunologic changes, tumor-associated antigens, and progress in immunotherapy in patients with head and neck cancer. (Author abstract) (220 Refs)

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DETECTION/ CHARACTERIZATION/ ISOLATION

1. NUCLEOLAR ANTIGENS OF HUMAN TUMORS.

Busch H, Busch RK, Chan PK, Kelsey D, Takahashi K
Dept. Pharmacology, Baylor Coll. Medicine, Houston, TX, 77030
Methods Cancer Res; 19:109-178 1982

Nucleolar antigens (NA), which may reflect unique functions in human cancer cells and have potential immunodiagnostic use, are discussed in this review of the evaluation, identification, isolation, and functional analysis of NA from human cancer cells. Immunofluorescent microscopy, tumor specificity, adsorption of antibodies, and NA from specific tissues are described. Characterization methods include isoelectric focusing, densitometric scanning, column chromatography, electrophoresis, affinity gel purification, and amino acid analysis. Quantitative assays are reviewed, including preparation of nuclear extracts and solid phase absorbents, and enzyme immunoassay, with discussions of immunoadsorption and antigen specificity. Localization of the NA in electron micrographs is described using the example of antigen(s) in nucleoli of HeLa cells treated with adriamycin by specific immunoperoxidase-antiperoxi-

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dase (PAP) reaction. Possible functions of the NA, which have been found in 95% of malignant tumor samples studied but in few if any benign tumors, are discussed. (40 Refs)

2. BIOCHEMICAL CHARACTERISATION OF LEUKAEMIA-ASSOCIATED ANTIGEN P24 DEFINED BY THE MONOCLONAL ANTIBODY BA-2.

Newman RA, Sutherland DR, Lebien TW, Kersey JH, Greaves MF
Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England
Biochim Biophys Acta; 701(3):318-327 1982

The leukemia-associated cell surface antigen p24/BA-2 is a single polypeptide chain with a molecular wt of 24,000. Treatment with glycosidases or exposure of cells to tunicamycin failed to show any change in the mol wt of the antigen when examined by SDS-polyacrylamide gel electrophoresis. In addition, it failed to bind to lectin affinity columns of concanavalin A, lentil lectin or Ricinus communis lectin. This is consistent with the absence of N-asparagine linked oligosaccharide chains on the antigen. Pulse-chase labeling of protein p24 shows a post-translational modification resulting in a mol wt increase of approx 500-1,000. Alkaline treatment resulted in a decrease in mol wt of approx the same amount, suggesting that p24 may contain some O-glycosidically linked oligosaccharide. Protein p24 has a basic pI of 7.3 which is unchanged after neuraminidase treatment. Protein p24/Ba-2 cannot be labeled by either the lipophilic photoactivatable nitrene reagent, hexanoyldiiodo-N-(4-azido-2-nitrophenyl)tyramine, or with [32P]phosphate. This suggests that the molecule is non-integral in nature and that it does not form an intimate association with the lipid matrix. Identical mol wt, when reduced and non-reduced antigens were compared, suggest that it contains no internal disulfide linkages and failure to detect any other band on gradient gel SDS-polyacrylamide gel electrophoresis from 5-15% suggests that it is not strongly associated with any other structure. (Author abstract) (31 Refs)

3. IDENTIFICATION AND PARTIAL CHARACTERIZATION OF SPECIFIC ANTIGEN ON ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN.

Azuma E
Dept. Pediatrics, Mie Univ. Sch. Medicine, Tsu, Japan
Mie Med J; 31(1):57-65 1981

Identification and partial physical and chemical characterization of tumor-specific antigen (TSA) associated with acute lymphoblastic leukemia (ALL) are reported. Peripheral blood samples were obtained from patients with clinically and cytologically diagnosed ALL upon admission to the hospital. Cells were classified as T cell, B cell, or non-T non-B ALL. Also studied were Molt-4B (T cell ALL) and Raji (B cell ALL) cell lines. Rabbit antisera were raised against ALL cells and purified. In indirect immunofluorescence tests, the rabbit antisera reacted with 34/37 non-T non-B samples, 1/4 T cell samples, and no B cell, acute myeloblastic leukemia, chronic lymphoblastic leukemia, chronic myeloblastic leukemia, or Molt-4B samples. The antisera did not react with fetal thymocytes, fetal bone marrow, cord blood, neuroblastoma cells, or normal bone marrow cells. TSA from leukemic cells was extracted by the 3 M-KCl method. In immunoprecipitation tests antiserum reacted with a component of mol wt of 80,000-90,000 daltons. Extracts from non-ALL cells did not react with antisera. The isoelectric point of the TSA was pH 4-5. Results indicate that non-T non-B and a limited number o T cell ALL have a TSA of mol wt 80,000-90,000 daltons. (18 Refs)

4. AN IMMUNOCYTOCHEMICAL STUDY OF THE DISTRIBUTION OF EPITHELIAL MEMBRANE ANTIGEN IN NORMAL AND DISORDERED SQUAMOUS EPITHELIUM.

Sloane JP, Ormerod MG, Carter RL, Gusterson BA, Foster CS
Dept. Histopathology, Royal Marsden Hosp., Sutton, Surrey SM2 5PX, England
Diagn Histopathol; 5(1):11-17 1982

Epithelial membrane antigen (EMA), a membrane component which can be detected by an immunohistochemical procedure using Mayer's hemalum counterstain, was analyzed in preparations of normal adult squamous epithelium and in tissues from patients with in situ squamous carcinoma, infiltrating carcinoma and other malignant tumors, dysplastic and nondysplastic epithelium adjacent to infiltrating squamous carcinoma, benign tumors and related non-neoplastic disorders, and squamous metaplasia. All normal tissues were negative for EMA; staining of other tissues was uniformly positive in squamous carcinoma of the larynx and bronchus and in squamous metaplasia, but staining was variable in the other tissues. The intensity of staining was usually greater in the superficial tissue layers. EMA may have a protective function, as indicated by the tendency to concentrate in superficial layers, the superficial half of cells, or in or near zones of inflammation. EMA may be useful in differential diagnosis of some skin tumors. (16 Refs)

5. HUMAN MELANOMA-ASSOCIATED ANTIGEN P97 IS STRUCTURALLY AND FUNCTIONALLY RELATED TO TRANSFERRIN.

Brown JP, Hewick RM, Hellstrom I, Hellstrom KE, Doolittle RF, Dreyer WJ
Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
Nature; 296(5853):171-173 1982

Cell surface glycoprotein p97 (mol wt 97,000), in SK-MEL 28 melanoma cells, was purified by affinity chromatography with monoclonal antibody, followed by sodium dodecyl-polyacrylamide gel electrophoresis. The N-terminal acid sequence was determined with the use of a new, highly sensitive protein sequencer. Amino acid sequence analysis of purified p97 yielded a sequence of 12 residues at the N-terminus. Computer search of the Newat amino acid sequence library showed this sequence was homologous to the N-terminal sequence of transferrin: 7 of the 12 residues were identical. This homology is considered significant for two reasons: first, the two least common amino acid residues, Trp and Cys, are among those conserved, and second, six of the seven conserved residues are also conserved at the N-terminus of lactotransferrin. This homology was confirmed by the observation that antiserum to denatured p97 cross-reacted with denatured transferrin and lactotransferrin. p97 was also functionally related to transferrin and lactoferrin in that it binds iron. The presence of p97 on certain cell types suggests that its function may be translocation of iron. (15 Refs)

6. A CELL-SURFACE ANTIGEN WHICH IS PRESENT IN THE GANGLIOSIDE FRACTION AND SHARED BY HUMAN MELANOMAS.

Yeh MY, Hellstrom I, Abe K, Hakomori S, Hellstrom KE
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Int J Cancer; 29(3):269-275 1982

We have raised a hybridoma, 4.2, which forms an IgM antibody to an antigen expressed on cultivated cells from most human melanomas, more infrequently on cells from other human tumors, and very weakly on cultivated fibroblasts, T cells and B cells. The antigen can be detected in biopsy material of human melanoma and, in smaller amounts, in fresh samples of normal human lung and kidney. Preliminary biochemical characterization indicates that it is associated with the ganglioside fraction. We feel that the antigen (referred to as 4.2) has a sufficient degree of tumor specificity to be rated as a human melanoma-associated antigen. (Author abstract) (24 Refs)

7. CELL SURFACE MODULATION IN MAMMARY CANCER.

Thompson K
Bruce Lyon Memorial Res. Lab., Children's Hosp. Medical Center, Oakland, CA, 94609
The Handbook of Cancer Immunology: Volume 8- Tumor Antigens: Structure and Function. Waters H, ed. New York, STPM Garland Press, 418 pp., 1981.

Studies of the cell surface modulation which accompanies malignant transformation in mammary cancer are reviewed. Evidence for cell surface antigens (CSAs) of mouse and rat mammary tumors has not shown whether neoplastic transformation is associated with distinct tumor-specific antigens. Virus-induced mouse mammary tumors contain virus-specific antibodies, which are also present in normal mammary cells and nonmammary tissues. In rats with carcinogen-induced mammary tumors, the tumor loses an organ-specific antigen at the time of spontaneous dissemination. The experimental mammary tumors may also show gene derepression, which leads to the expression of abnormal differentiation antigens and/or fetal-type antigens. The tumors can acquire new CSAs not found in the tissue of origin and can acquire or lose CSAs already present in normal cells. Neoplastic transformation is a complex process, especially with regard to the cells which become neoplastic and the influence of host factors (genetic, hormonal, or immunologic). Interaction of these factors determines the malignant state. (283 Refs)

8. THE USE OF CELL MEMBRANES TO ASSESS PHENOTYPIC EXPRESSION.

Ceriani RL
Bruce Lyon Memorial Res. Lab., Children's Hosp. Medical Center, Oakland, CA, 94609
The Handbook of Cancer Immunology: Volume 8- Tumor Antigens: Structure and Function. Waters H, ed. New York, STPM Garland Press, 418 pp., 1981.

The specificity, distribution, properties, and levels of expression of milk fat globule membrane antigens in human and mouse mammary epithelial cells are discussed. When more is known about these 'antigens' cell surface expressions at the molecular level, they can be used to study cell-cell interactions, tissue invasiveness, and the dissemination of mammary neoplasms. It is emphasized that the term 'tumor antigens' is inappropriate for components that are normally expressed in an earlier stage of differentiation, which reappear in neoplastic cells. Neoplastic transformation leads to a protean instability of the antigenic phenotype. The appearance of early differentiation components and the gradual disappearance of the mature components seem to be strictly linked. Further research is needed to improve the culture of human breast epithelial tissues and identify their mammary epithelial origin and particularly their neoplastic phenotype. Normal mammary epithelial cells grow readily in vitro, but neoplastic cells do not. (88 Refs)

9. CHARACTERIZATION OF A HUMAN LUNG TUMOR-ASSOCIATED ANTIGEN AND DEVELOPMENT OF A RADIOIMMUNOASSAY.

Braatz JA, Scharfe TR, Princler GL, McIntire KR
Frederick Cancer Res. Facility, Building 560, Room 3152, Frederick, MD, 21701
Cancer Res; 42(3):849-855 1982

A human lung tumor-associated antigen (LTA), previously isolated from a small cell carcinoma, was further studied after labeling with N-succinimidyl-3-(4-hydroxy-5 [125I]iodophenyl)propionate. Two immunoreactive forms of the labeled antigen were isolated. components, referred to as LTA-I and LTA-II in order of mobility, were judged homogeneous by gel electrophoresis, G-200 gel filtration, size exclusion high-performance liquid chromatography, and sedimentation velocity analysis. The latter three techniques produced identical profiles for both forms of the LTA. Sephadex chromatography and high-performance liquid chromatography analyses indicated the mass of the antigens to be approx 140,000 to 150,000 daltons with a D20,w of 4.2 to 4.3 x 10(-7) sq cm/sec. The S20,w values for both were 4.5 to 4.6S. Sodium dodecyl sulfate gel electrophoresis of LTA-II gave a single component with a mol wt of 81,700, while LTA-I had a major component identical in size to LTA-II and two minor components with mol wt of 50,000 and 27,700, respectively. The isoelectric point of LTA-II (peaks at pH 2.6 and 3.2) generally was more acidic than LTA-I (major component centered at pH 4.7, minor component centered at pH 3.1). A radioimmunoassay, with a useful detection range of from 1 to 100 ng/ml, was developed with LTA-I. This assay was used to determine the concentration of LTA in the sera of normal and lung cancer patients. Fifteen normal sera had a mean of 17 +-22 (SD) ng/ml, with none greater than 83 ng/ml (+3 SD). Thirteen lung cancer patients with Stage I (ie, localized disease) had a mean of 187 +-219 ng/ml, with the means for 7 of 13 patients being greater than 83 ng/ml; 15 lung cancer patients with Stage III, more extensive disease, had a mean of 277 +-252 ng/ml, with the means for 12 of 15 patients being greater than 83 ng/ml. This antigen may be useful for the early detection or monitoring of lung cancer. (Author abstract) (21 Refs)

10. IDENTIFICATION AND PURIFICATION OF A HUMAN LUNG TUMOR-ASSOCIATED ANTIGEN FROM A PRIMARY LUNG TUMOR.

Princler GL, McIntire KR, Braatz JA
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Cancer Res; 42(3):843-848 1982

A human lung tumor-associated protein has been purified from an extract of a human small cell carcinoma of the lung and shown by Ouchterlony double diffusion analysis to be antigenically identical to a component which was previously demonstrated in 84 of 98 lung tumor extracts of all histological types but absent from extracts of normal adult and fetal lung, other normal tissues, and tumors of other organs. These studies utilized xenoantisera raised against a pool of lung tumor extracts which were exhaustively adsorbed with normal serum and tissue extracts. A radical immunodiffusion assay developed for the antigen permitted is quantitation throughout the course of isolation. Purification was accomplished by ion-exchange chromatography, gel filtration and affinity immunoadsorption. By ion-exchange chromatography, the proteins appeared to be quite heterogeneous, with immunological reactivity detected in three different peaks. However, all the active components were immunologically identical. Gel filtration of the major antigenic component from diethylaminoethyl cellulose similarly demonstrated a further fractionation into several active, immunologically identical forms. These results suggest a charge-size isomeric relationship among the various forms, all of which possess a common and identical antigenic site. The major component was isolated throughout the purification scheme. The final product represented 9% of the input activity, produced a single, although broad, protein-staining region on 7% polyacrylamide gels which was coincident with antigenic activity, and exhibited immunological identity with the antigen in the crude extract as well as with that in an extract from another lung tumor. (Author abstract) (21 Refs)

11. CHEMICAL SYNTHESIS OF ALPHA-L-FUCOPYRANOSYLCERAMIDE AND ITS ANALOGUES AND PREPARATION OF ANTIBODIES DIRECTED TO THIS GLYCOLIPID.

Yoshino T, Watanabe K, Hakomori S
Dept. Chemistry, International Christian Univ., Mitaka, Tokyo, Japan
Biochemistry; 21(5):928-934 1982

A novel glycolipid, alpha-L-fucopyranosylceramide, was previously isolated and characterized from metastatic human adenocarcinoma. For further investigation of the pathobiological significance of this glycolipid with its specific antibodies, the antigen glycolipid alpha-L-fucopyranosylceramide was chemically synthesized by Konigs-Knorr-type condensation of 2,3,4-tri-O-benzyl-alpha-L-fucopyranosyl bromide and a ceramide, followed by removal of benzyl groups by catalytic hydrogenation. Alpha-L-Fucopyranosyl-N-palmitoylethanolamine and 2,3,4-tri-O-benzyl-alpha-L-fucopyranosylsphingosine were also synthesized. The antibodies prepared against a synthetic alpha-L-fucopyranosylceramide included in liposome reacted very well with the synthetic as well as the natural alpha-L-fucopyranosylceramide isolated from human adenocarcinoma, but the kinetics of the complement-dependent liposome lysis and the complement fixation pattern with the synthetic fucosylceramide were significantly different from those with the natural fucosylceramide. The natural fucosylceramide showed a much weaker immunogenicity than the synthetic fucosylceramide. The remarkable difference in liposome lysis, complement fixation, and immunogenicity between the synthetic and the natural fucosylceramide must be due to the difference in ceramide structures. The results indicate that the strength of antigenicity and immunogenicity of glycolipids may greatly depend on ceramide structure, whereas the specificity is solely determined by the sugar moiety. The anti-alpha-L-fucosylceramide antibodies display cross-reactivity with galactosylceramide, ceramide, and liposome alone that was eliminated by absorption with galactosylceramide liposomes. (Author abstract) (14 Refs)

12. DISTRIBUTION OF NOVIKOFF ASCITES HEPATOMA ANTIGENS P39 AND P49 IN VARIOUS TUMORIGENIC CELL LINES.

Schmidt WN, Hnilica LS
Dept. Biochemistry, Vanderbilt Univ. Cancer Center, Nashville, TN, 37232
Cancer Res; 42(4):1441-1445 1982

This study investigates the specificity of two antigenic proteins with mol wt of 39,000 and 49,000 respectively (p39 and p49), present in Novikoff ascites hepatoma. Chromatins and cytosol fractions were assayed from a number of tumorigenic cell lines by identifying antigenic species immunologically on nitrocellulose transfers containing proteins separated electrophoretically. Immunoreactivity was confirmed with complement-fixation. Although the p49 antigen was present only in Novikoff ascites hepatoma and a tissue culture line derived from these ascites cells, the p39 antigen was found in every carcinoma cell line examined. In contrast, neither antigen was present in a representative sarcoma, fibrosarcoma, or Walker 256 carcinosarcoma. These results suggest that the p39 antigen is a protein specific for malignant cells derived from the epithelium. The overall expression of the p39 antigen by the various cell lines examined did not appear to be influenced by in vivo or in vitro growth of homologous cell lines. This latter feature suggests that the p39 antigen is a stable, possibly structural component of neoplastic cells. (Author abstract) (29 Refs)

13. PRODUCTION OF MONOCLONAL ANTIBODY ALPHAPRO3 RECOGNIZING A HUMAN PROSTATIC CARCINOMA ANTIGEN.

Ware JL, Paulson DF, Parks SF, Webb KS
Dept. Surgery, Div. Urology, Duke Univ. Medical Center, Durham, NC, 27710
Cancer Res; 42(4):1215-1222 1982

The monoclonal antibody alphaPro3 recognizes an antigen concentrated in human primary prostatic carcinoma tissue removed surgically. Although the antigen was detectable in extracts of human normal and malignant nonprostatic tissue, as well as in benign prostate tissue, quantitative absorption analysis revealed a substantially greater quantity of the antigen in malignant prostate tissue. The antigen recognized by alphaPro3 in primary prostatic carcinoma has an apparent nonreduced molecular weight of 175,000 and an apparent subunit molecular weight of 54,000. This antigen, p54, appears to be present on the surface of cultured prostatic tumor cells of the PC-3 cell line, but its location in vivo has been defined. Successful competition between alphaPro3 and prostatic carcinoma patient serum immunoglobulin for a Mr 54,000 antigen (reduced molecular weight) present in prostatic carcinoma tissue extract suggests that p54 may play a significant role in the immunobiology of prostatic carcinoma. AlphaPro3 has potential as a sensitive probe for an antigen relevant to human tumor biology. (Author abstract) (46 Refs)

14. PROSTATE ANTIGEN OF HUMAN CANCER PATIENTS.

Wang MC, Kuriyama M, Papsidero LD, Loor RM, Valenzuela LA, Murphy GP, Chu TM
Dept. Diagnostic Immunology Res. and Biochemistry, Roswell Park Memorial Inst., Buffalo, NY, 14263
Methods Cancer Res; 19:179-197 1982

A new prostate-specific antigen (PA), which is distinct from prostate acid phosphatase, is described. Procedures for identification of PA in the prostate, in prostatic fluid and seminal plasma, and for determining PA concentration and localization are discussed. Enzyme-linked immunoabsorbent assay has demonstrated the presence of PA in prostatic carcinoma metastasized to lymph node (LNCaP) and lumbar vertebra (PC-3) cells and in their spent culture fluids, but not in cultured cells from several other lines. Expression of PA was retained in brain DU-145 cells and LNCaP cells implanted in athymic nude mice, but not in other lines similarly transplanted. Several isomeric varieties of PA have been extracted from human prostate and seminal plasma, and from circulating PA in human serum. Circulating PA levels in prostatic carcinoma patients and those with benign prostatic hypertrophy are higher than in normal individuals. Serum PA levels of cancer patients have proven useful in predicting survival time, monitoring clinical course, and predicting early recurrence. (38 Refs)

15. IMMUNOPRECIPITATION OF MEMBRANE PROTEINS OF CULTURED HUMAN SARCOMA CELLS.

Grofova M, Forchhammer J, Lizonova A, Popovic M
Cancer Res. Inst., Slovak Acad. Sciences, 812 32 Bratislava, Czechoslovakia
Neoplasma; 28(6):633-645 1981

Human sarcoma associated antigens (HSAA) have previously been identified by indirect immune fluorescence in human sarcoma cells in culture using sera from patients bearing different types of sarcoma. To further characterize these HSAA, surface proteins of cultured cells were labeled with 125Iodine, [3H]-glucosamine and [35S]-methionine and solubilized. After immunoprecipitation labeled proteins were detected in immune complexes by SDS polyacrylamide gel electrophoresis and autoradiography, which allowed comparison with antigens described by other groups. A surface protein (Mr 96,000) was precipitated with sera from sarcoma bearing patients, and two glycoproteins (Mr 115,000 and 85,000) were preferentially precipitated with antisera from rabbits immunized with membranes from two human sarcoma cell lines. At least two of these proteins were found in each of five human sarcoma cell lines studied (U-4SS, U-3930S, U-20S, B-5GT and B-6FS). None of the proteins were precipitated with three human control sera, and only occasionally a faint band was observed in immunoprecipitates from control cells (B-25F, B-41B, B-42FC, U-2S, and U-393S) with the immune sera. These proteins are probably some of the antigens responsible for the immune fluorescence observed in determination of HSAA. However, purification of the proteins and competition experiments are needed before this can be finally established. (Author abstract) (26 Refs)

16. FC RECEPTORS OF MOUSE CELL LINES. II. IGG BINDING SPECIFICITY AND IDENTIFICATION OF THE FC RECEPTOR ON A LYMPHOID LEUKEMIA.

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J Immunol; 128(4):1825-1831 1982

We determined the binding specificity of the Fc receptors on the murine lymphoid leukemia, L1210, which bears several surface antigens characteristic of B cells and B cell precursors. L1210 possesses an Fc receptor that binds monomer IgG of the IgG1, IgG2a, and IgG2b subclasses with low affinity, whereas aggregated IgG of these subclasses is bound comparatively well. There was no detectable binding of monomer or aggregated IgG3. Although direct binding of monomer IgG was difficult to demonstrate, monomer inhibition of aggregate binding was found at monomer concentrations in excess of 0.2 mg/ml. There was cross-competition between monomers and aggregates of all three subclasses, indicating that all were binding to the same Fc receptor. Isolation and characterization of the Fc receptor of L1210 was accomplished by affinity chromatography of the radiolabeled cell lysate over columns of Sepharose 4B coupled to various IgG and control proteins. A single protein, with an approx mw of 60,000, was found to specifically bind to the Fc portion of IgG. This protein was demonstrated in the acetic acid and SDS eluates from columns coupled to monomer, aggregated, or antigen-complexed IgG, but was not seen in eluates from F(ab')2 columns or from eluates of IgG columns that received the lysates of Fc receptor-negative cells. The 60-kd Fc binding protein was also demonstrated in the SDS eluates from affinity columns of Sepharose 4B coupled to myeloma proteins of mouse IgG1, IgG2a, and IgG2b subclasses. These studies indicate that in contrast to mouse macrophage-like cell lines that possess separate IgG subclass specific Fc receptors, L1210, a murine leukemia of possible B cell lineage, possesses a single Fc receptor with distinct binding and structural characteristics. (Author abstract) (40 Refs)

17. BIOCHEMICAL CHARACTERIZATION AND CELLULAR DISTRIBUTION OF A POLYMORPHIC, MURINE CELL-SURFACE GLYCOPROTEIN EXPRESSED ON LYMPHOID TISSUES.

Trowbridge IS, Lesley J, Schulte R, Hyman R, Trotter J
Dept. Cancer Biology, Salk Inst., Post Office Box 85800, San Diego, CA, 92138
Immunogenetics; 15(3):299-312 1982

A murine leukocyte surface glycoprotein (Mr = 95,000) has been defined by means of xenogeneic monoclonal antibodies. In normal hematopoietic tissues, the glycoprotein is found in highest amounts in the bone marrow. Flow cytometric analysis shows that essentially all bone-marrow cells express the glycoprotein and that it is a major component of a subpopulation of cells containing predominantly granulocytic precursors. In contrast, only about 5% of thymocytes express sufficient glycoprotein to be detected by flow cytometric analysis, although under stringent conditions up to 20% of thymocytes are susceptible to complement-mediated cytotoxicity using a monoclonal antibody against the glycoprotein. Functional assays showed that both prothymocytes and colony forming unit-spleen express the glycoprotein which is broadly distributed on murine hematopoietic tumor cell lines. However, although some Thy-1+ (T) cell lymphomas express large amounts of the glycoprotein, others do not express detectable quantities of the molecule. The glycoprotein is not restricted to hematopoietic cells and can be detected on lung, kidney, brain, and liver as well as cultured fibroblasts. Monoclonal antibodies against the glycoprotein cross-react with an antigen present on human cells. As described in the accompanying paper, the glycoprotein exists in two antithetical allelic forms and we show that it is identical to a polymorphic surface molecule independently characterized by Colombatti and co-workers. (Author abstract) (41 Refs)

18. FUNCTIONALLY DIFFERENT SUBPOPULATIONS OF MOUSE MACROPHAGES RECOGNIZED BY MONOCLONAL ANTIBODIES.

Sun D, Lohmann-Matthes M
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Eur J Immunol; 12(2):134-140 1982

Four rat anti-mouse macrophage monoclonal antibodies are described. Three of them are highly specific for macrophages, and one cross-reacts with granulocytes. All four antibodies do not react with membrane antigens shared by all macrophages, but with antigens present only on subpopulations of 20-50% of the cells. All antibodies are directly or indirectly cytotoxic for macrophages. The subpopulations defined by these antibodies can be correlated with certain macrophage functions. Thus, antibody M43 eliminates macrophages that are activated by lymphokine to cytotoxicity. Antibodies M43 and M57 eliminate macrophages that kill antibody-coated tumor targets, and clone 102 (strictly macrophage-specific) eliminates natural killer cells. Only M143, reacting with 10-30% of macrophages, has not yet been correlated with any function. With the use of these antibodies, cells of the macrophage lineage with specific functions can be recognized and eliminated for a given population. (Author abstract) (22 Refs)

19. MAC-2, A NOVEL 32,000 M4 MOUSE MACROPHAGE SUBPOPULATION-SPECIFIC ANTIGEN DEFINED BY MONOCLONAL ANTIBODIES.

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J Immunol; 128(3):1221-1228 1982

Two monoclonal antibodies, M3/31 and M3/38, were obtained by fusion of mouse myeloma cells with rat spleen cells immunized to immunoadsorbent-purified macrophage glycoproteins. Co-precipitation experiments show that antigenic determinants recognized by these two antibodies reside on the same molecular species, termed Mac-2. Mac-2, an antigen of 32,000 Mr, is synthesized by and expressed on the surface of thioglycollate-elicited macrophages as shown by [35S]-methionine and 125I labeling. Saturation binding experiments show that thioglycollate-elicited macrophages express 1.7 x 10(5) Mac-2 sites/cell. Thioglycollate-elicited macrophages are strongly absorptive for 125I-labeled M3/38 MAb. Kidneys are also absorptive; however, evidence is presented pointing to the nonspecificity of this absorption. Lymph node and thymus are negative, whereas spleen and bone marrow are weakly absorptive, probably due to stromal cells. Nonlymphoid tissues, such as lung, liver, heart, and brain, exhibit slight or no absorbing capacity. Cell suspensions from spleen, bone marrow, thymus, and peripheral lymph node are greater than 99% Mac-2-by immunofluorescent flow cytometry. In contrast, thioglycollate-elicited macrophages are greater than 96% strongly positive for Mac-2. Only 20% of peptone-elicited cells are weakly positive, whereas resident peritoneal macrophages and other macrophages elicited by Listeria monocytogenes, Con A, or LPS are greater than 98% negative. SDS-PAGE of [35S]-methionine-labeled Mac-2 shows that thioglycollate-elicited macrophages synthesize 10-to 30-fold more Mac-2 than other peritoneal macrophage subpopulations, whereas all types of peritoneal macrophages synthesize and express on their surfaces similar amounts of the Mac-1 antigen. Mac-2 antigen is therefore induced in macrophages only in response to specific differentiative signals. (Author abstract) (30 Refs)

20. THE MASKING OF CANCER CELL SURFACE ANTIGENS.

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The Handbook of Cancer Immunology: Volume 8- Tumor Antigens: Structure and Function. Waters H, ed. New York, STPM Garland Press, 418 pp., 1981.

One major type of tumor antigen masking at tumor cell surfaces involves the masking of cryptantigens by sialic acid (SA) residues in terminal positions on carbohydrate chains. This may be involved in escape and control mechanism. Immunotherapy using neuraminidase can be used to expose SA-masked cryptantigens. Another type of tumor antigen masking at tumor cell surfaces involves a steric hindrance phenomenon caused by large endogenous glycoprotein (GLP) molecules. This may be involved in tumor allotransplantability and dissemination. The characteristics of GLPs which may be involved in antigenic masking of mouse and rat ascites mammary carcinomas are discussed. It is possible that mammalian tumor cells may utilize some of the protective mechanisms found in bacterial, parasitic, or mycoplasma infections. (133 Refs)

21. TERATOCARCINOMA CELL ADHESION: IDENTIFICATION OF A CELL-SURFACE PROTEIN INVOLVED IN CALCIUM-DEPENDENT CELL AGGREGATION.

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Cell; 28(2):217-224 1982

Teratocarcinoma cells have a Ca++-dependent cell-cell adhesion site (t-CDS) that is unique in being inactivated with trypsin in the absence of Ca++ but not in the presence of Ca++. Fab fragments of antibodies raised against teratocarcinoma F9 cells dissociated by treatment with trypsin and calcium (anti-TC-F9) inhibit the aggregation of teratocarcinoma cells mediated by t-CDS. This inhibitory effect of Fab is removed when anti-TC-F9 is absorbed with F9 cells treated with trypsin and calcium (TC-F9), but not when it is absorbed with F9 cells treated with trypsin and EGTA (TE-F9). Comparisons of cell-surface antigens reactive to anti-TC-F9 in TC-F9 cells with those in TE-F9 cells reveal that only one component, with an approx mol wt of 140,000 (p140), is detected specifically on the surface of TC-F9 cells. When TC-F9 cells are retrypsinized in the absence of Ca++, a substance with an approx mol wt of 34,000 (p34) is released that can neutralize the aggregation-inhibitory effect of the Fab. This p34 interferes with the immunoprecipitation of p140 with anti-TC-F9, suggesting that p34 is a tryptic fragment of p140. Anti-TC-F9 Fab causes the dissociation of the monolayers of teratocarcinoma cells. This effect is removed by absorption of the Fab with p34 as well as with TC-F9 cells, but not with TE-F9 cells. These results suggest that p140 is essential for the function of t-CDS, and that this is an actual cell-adhesion molecule active in the establishment of monolayers of teratocarcinoma cells. (Author abstract) (37 Refs)

IMMUNOLOGICAL STUDIES

22. HUMAN TUMOUR ANTIGENS DEFINED BY CYTOTOXICITY AND PROLIFERATIVE RESPONSES OF CULTURED LYMPHOID CELLS.

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Nature; 296(5855):359-361 1982

Methods of initiating continued lymphocyte cultures (CLC) having specific antitumor reactivity are described. Blood lymphocytes were obtained from cancer patients on the morning of surgery. The lymphocytes were grown in optimal quantities of different conditioned media containing interleukin-2 (IL-2) reactivity. The resulting cultured cells were tested for cytotoxicity against a range of target cells, including freshly isolated autologous and allogeneic tumor cells. The possible presence of natural killer (NK) cells was investigated with CLC against K562 cells. CLC showed cytotoxicity against both autologous and allogeneic tumor targets, and high levels of cytotoxicity against K562 cells were found in some conditioned media. No evidence of selective reactivity against the autologous tumor alone was found. Often, cytotoxicity against allogeneic tumors of unrelated types exceeded that against autologous tumors. Use of positive mixed lymphocyte-tumor cultures (MLTC) was critical to the experiments; cultures could be initiated from MLTC-negative individuals, but no specific reactivity was found in these CLC. Isolation of blast cells was necessary;

without isolation, the cultured cells showed features of polyclonal T-cell activation and high NK activity. With the MLTC-CLC, selective lysis of autologous tumors and restimulation in primed lymphocyte test assays were demonstrated. (21 Refs)

23. RELATIONSHIP OF CELL-CYCLE EXPRESSION OF IA-LIKE ANTIGENIC DETERMINANTS ON NORMAL AND LEUKEMIA HUMAN GRANULOCYTE-MACROPHAGE PROGENITOR CELLS TO REGULATION IN VITRO BY ACIDIC ISOFERRITINS.

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Dept. Developmental Hematopoiesis, Sloan-Kettering Inst. Cancer Res., New York, NY, 10021
J Clin Invest; 69(3):632-642 1982

An association has been established between human Ia-like (Ia) antigenic determinants, expression during DNA synthesis on granulocyte-macrophage colony forming cells (CFU-GM) and the regulatory action of acidic isoferritins in vitro. Treatment of human bone marrow cells with monoclonal-anti-Ia-like (Ia) plus complement inhibited colony and cluster formation by approx 50% but did not affect pre-CFU-GM. Reduction of colonies and clusters was similar whether bone marrow cells were exposed to anti-Ia plus complement, high specific activity tritiated thymidine (3HTdr) or acidic isoferritins. No further decrease was apparent with 3HTdr or acidic isoferritins after Ia-antigen+ CFU-GM were removed, or with anti-Ia plus complement or acidic isoferritins after DNA synthetic phase (S-phase) CFU-GM were removed. Anti-Ia, without complement, did not reduce colony or cluster formation but did block the inhibitory action of acidic isoferritins. A relationship existed between Ia antigens and the activity of acidic isoferritins in the following ways: (a) The apparent loss of Ia-antigens from CFU-GM by 5 hr in culture at 37 C, but not at 27 C or 4 C, was associated with nonresponsiveness to inhibition with acidic isoferritins, (b) Ia-antigen-, noncycling pre-CFU-GM that were insensitive to acidic isoferritins could generate a population of Ia-antigen+ cycling CFU-GM in vitro that were responsive to inhibition by acidic isoferritins, and (c) nondetectability of Ia-antigens on CFU-GM from patients with leukemia was associated with nonresponsiveness to inhibition by acidic isoferritins. These results implicate Ia-antigen+ progenitor cells in the regulation of myelopoiesis in vitro and demonstrate that absence of Ia-antigens on patient CFU-GM is associated with imbalances in normal regulatory interactions in vitro. These findings may be of relevance to normal regulation and to the progression of leukemia. (Author abstract) (30 Refs)

24. INVOLVEMENT OF HUMAN MEMBRANE-ASSOCIATED COMPLEMENT COMPONENTS IN THE ROSETTE FORMATION BETWEEN MARMOSET RED BLOOD CELLS AND HUMAN LEUKOCYTES.

Teillaud JL, Goujet-Zalc C, Fontaine M, Braun C, Mahouy G
Institut de Recherches sur les Maladies du Sang,, Laboratoire des Interactions lymphocytaires Hopital Saint-Louis, 75475 Paris Cedex 10, France
Cell Immunol; 66(2):254-268 1982

The majority of human monocytes, a subpopulation of B lymphocytes, and all B lymphoblastoid cell lines (B-LCL) tested but one form rosettes with Marmoset red blood cells (MaRBC). None of the human peripheral T cells, T-LCL, and B chronic lymphoid leukemia cells (B-CLL) used bind to MaRBC. The binding could not be correlated with any membrane markers or antigens present on cultured cells or peripheral blood leukocytes (PBL). Blocking of the rosette formation by preincubation of MaRBC with purified human complement (C) components and cobra venom or by pretreatment of leukocytes and cultured cells with antisera to human C components suggested that membrane-associated C components present on PBL or B-LCL are involved in the binding to MaRBC. (Author abstract) (35 Refs)

25. IN VITRO CELLULAR IMMUNE REACTIVITY OF SOLUBLE ANTIGENS OBTAINED FROM CULTURED LEUKEMIC CELLS IN CHRONIC MYELOID LEUKEMIA.

Khare AG, Advani SH, Gangal SG
(c/o Gangal) Immunology Div., Cancer Res. Inst., Bombay 400 012, India
Indian J Exp Biol; 19(6):524-527 1981

The preparation of potent antigenic substances from leukemia cells by culturing in vitro for various time periods was investigated. Antigens prepared from uncultured cells produced significant inhibition of leukocyte migration in 9/11 tests. Leukemic cells cultured for 24 hr yielded antigens with very high lymphocyte transformation activity in 7/11 tests. Chronic myeloid leukemia leukocyte/lymphocyte samples tested with cells cultured for 48 and 72 hr showed a progressive reduction in the number of positive reactions. Leukemic cell antigens prepared after 24 hr of incubation showed greater activity than antigens prepared from uncultured cells. (16 Refs)

26. THE RELATIONSHIP BETWEEN T LYMPHOCYTE SUBSETS AND IA-LIKE ANTIGEN POSITIVE NONLYMPHOID CELLS IN EARLY STAGES OF CUTANEOUS T CELL LYMPHOMA.

Thomas JA, Janossy G, Path MR, Graham-Brown RA, Kung PC, Goldstein G
Dept. Immunology, Royal Free Hosp. Sch. Medicine, Pond St., London NW3 2QG, England
J Invest Dermatol; 78(2):169-176 1982

Immunofluorescence studies were carried out in cutaneous T cell lymphoma (mycosis fungoides) in order to analyze the microanatomical relationship of the different T lymphocyte subsets (inducer and suppressor/cytotoxic cell populations) to large nonlymphoid Langerhans-type and so-called 'indeterminate' or interdigitating cells. The conventional and mouse (monoclonal) antibodies were used in various combinations using fluorescein and rhodamine labeled second layers. In five of the seven cases studied the dermal infiltrate consisted of numerous T (HuTLA+) lymphocytes, 80-90% of which expressed the inducer phenotype (HuTLA+,OKT4+). Most of these cells formed close contact with large cells exhibiting large amounts of Ia-like antigens. These cells corresponded to the interdigitating and indeterminate cells in the sections. By contrast, only small numbers (10-20%) of T cells of suppressor/cytotoxic type (HuTLA+,OKT8+) were seen. These did not show a close affinity to the Ia-like antigen positive nonlymphoid component but appeared to have a predilection for the epidermis. Epidermal Langerhans cells, also strongly Ia-like antigen positive, were further defined by two monoclonal antibodies reacting with a cortical thymocyte antigen HTA-1. Although Langerhans cells are probably related to the Ia-like antigen positive dermal cells only a few of the abundant latter population were HTA-1+. In the remaining two cases, larger populations of OKT8+ (suppressor/cytotoxic) cells were seen and could be heralding a particularly benign course. These observations indicate a close functional relationship between the lymphoid and Ia-like antigen positive dermal cells during the pre-malignant phase of cutaneous T cell lymphoma. (Author abstract) (39 Refs)

27. MACROPHAGE ARGINASE, ARGININE CONSUMPTION, AND TUMORS.

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The Handbook of Cancer Immunology: Volume 7- Immune Function and Dysfunction in Relation to Cancer. Waters H, ed. New York, Garland STPM Press, 372 pp., 1981.

Many human and mouse tumors contain large macrophage populations and high levels of arginase (ARGase), which may be synthesized by the macrophages. In several experimental tumors, the growth rate is inversely related to the ARGase activity. Selective tumor growth inhibition by arginine depletion or ARGase treatment has been demonstrated. ARGase is immunosuppressive in vitro, but its involvement in immunosuppression in vivo has not been demonstrated. These findings suggest that ARGase may be involved in tumor immunity, and that ARGase synthesis by macrophages may be an early defense against tumor growth. This hypothesis could be tested by feeding tumor-bearing animals with arginine-deficient diets, with or without treatment by canavanine and nonantigenic ARGase. (73 Refs)

28. UNIVALENT ANTIBODIES KILL TUMOUR CELLS IN VITRO AND IN VIVO.

Glennie MJ, Stevenson GT
ARC Inst. Animal Physiology, Brabraham, Cambridge CB1 4AT, England
Nature; 295(5851):712-714 1982

The use of univalent antibodies to kill tumor cells in vitro and in vivo was studied. L2C cells were obtained from the blood of near-terminal guinea pigs bearing L2C lymphocytic leukemia. Two antibodies against L2C cells were raised in rabbits: one against the lambda chain of L2C surface immunoglobulin (anti-L) and one against idiotypic determinants of the surface immunoglobulin (anti-Id). Univalent Fab/c derivatives of both antibodies were prepared by digestion with thiol-free papain. Anti-L and anti-Id both bound to the surfaces of L2C cells in vitro, as shown by indirect immunofluorescence assay. Although parent bivalent anti-L and anti-ID underwent redistribution and endocytosis on the surface of L2C cells and rendered the cells resistant to lysis, the Fab/c derivatives did not. The derivatives were able to evoke complement-mediated lysis of L2C cells and did not tend to induce antigenic modulation. Both derivatives were superior to bivalent IgG in bringing about cell lysis. When tested in vivo against L2C tumor cells with a doubling time of approx 19 hr, Fab/c lengthened survival of guinea pigs by 10 days. Results indicate that bivalency of IgG plays an important role in allowing tumor cells to escape antibody-mediated lysis. Therapeutic value of univalent antibodies is suggested for treatment of human cancers. (20 Refs)

29. LIGAND-INDUCED ASSOCIATION OF SURFACE IMMUNOGLOBULIN WITH THE DETERGENT-INSOLUBLE CYTOSKELETAL MATRIX OF THE B LYMPHOCYTE.

Braun J, Hochman PS, Unanue ER
Dept. Pathology, Harvard Medical Sch., Boston, MA, 02115
J Immunol; 128(3):1198-1204 1982

Ligand binding is believed to induce surface immunoglobulin (Ig) to form a physical association with the underlying cell cytoskeleton. We investigated this interaction by use of nonionic detergents, which are known to dissolve membrane proteins but preserve a detergent-insoluble cytoskeletal residue. In the absence of ligand treatment, surface Ig in the B cell plasma membrane was fully dissolved by nonionic detergent; however, interaction with a ligand converted the receptor to a novel, detergent-insoluble state. The conversion of surface Ig to a detergent-insoluble form required receptor crosslinking but occurred independently of capping. Several types of experiments demonstrated that this form of Ig was not due to the size insolubility of immune complexes and involved a stable, noncovalent association of the receptor with the detergent-insoluble, cytoskeletal residue. Incubation of ligand-bound cells at 37 C promoted the degradation of surface Ig and the appearance of new, lower mw species, including a major soluble protein (50,000 daltons) that was antigenically related to surface Ig. These events corresponded to receptor endocytosis by several criteria (time course, temperature sensitivity, and energy dependence). Taken together, these results were consistent with the ligand-induced transmembrane attachment of receptors to the underlying cytoskeletal matrix followed by receptor internalization and catabolism. (Author abstract) (41 Refs)

30. ANTIBODY AND B CELL REGULATION OF IMMUNITY.

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Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
The Handbook of Cancer Immunology: Volume 9- Humoral Immunity in Relation to Cancer. Waters H, ed. New York, Garland STPM Press, 289 pp., 1981.

Antibody (Ab) formation by B-lymphocytes depends on a sequence of coordinated interactions of the B-cells with helper T-lymphocytes and macrophages. Antigen (Ag), binding to the surfaces of T- or B-cells (specifically) or macrophages (nonspecifically), may act as a triggering signal and a bridge between Ag-reactive cells. Ag-mediated bridging of B-cells and helper cells is sensitive to negative feedback control by Ab, apparently by two mechanisms. One mechanism, requiring high Ab levels, is based on the masking of Ag determinants, leaving them inaccessible to responsive lymphocytes. The other mechanism, operative in the presence of low Ab levels, presumably interferes with B-/helper cell cooperation without affecting Ag recognition by the immunocytes. The Ab-mediated inhibition of Ab production is reversible in factors present in tumor necrosis serum, which replaces helper T-cells and macrophages. An Ab may interfere with the appropriate B-/helper cell interaction by binding Ag via its Fc receptor (FcR) to FcR-containing (FcR+) cells, where the Ag is accessible to recognition by immunocytes but incapable of directing the appropriate association of B-cells with helper cells. Two mechanisms of Ab-mediated inhibition seem to be involved in cell-mediated immune reactions to tumors. One mechanism involves the masking by Ab of tumor Ag determinants. The other mechanism involves the formation of Ag-Ab complexes. It is suggested that the Ab may bind (via its Fc portion) a solubilized tumor Ag to the surfaces of FcR+ cells, thus diverting the cytotoxic lymphocytes from their tumor cell targets. (110 Refs)

31. A NEW MURINE LYMPHOCYTE ALLOANTIGEN, LY-21.2, MAPPING TO THE SEVENTH CHROMOSOME.

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Immunogenetics; 15(3):239-250 1982

Using a monoclonal antibody raised by fusing spleen cells from A/J mice, immunized with B10.A splenocytes and lymph-node cells, with a BALB/c myeloma, we have described a new surface alloantigen, Ly-21.2. Ly-21.2 is present in varying amounts in all lymphoid tissues, is not detectable in the brain, kidney, lung or erythrocytes, and is found in only trace amounts in the liver. Strain distribution studies showed that Ly-21.2 is present in all strains examined, including B10, except the A strain and segregation analysis of (A/J x B10)F2 mice showed that Ly-21.2 expression (1) is encoded by one gene and (2) is linked to albinism on chromosome 7. Studies performed on mice developing T-cell leukemia showed that, regardless of the etiologic agent, Ly-21.2 expression increases dramatically in mice with overt leukemia. In addition, preliminary studies suggest that expression of Ly-21.2 is linked to increased susceptibility of mice to Friend-virus-induced erythroleukemia. (Author abstract) (27 Refs)

32. SEROLOGIC IDENTIFICATION OF EARLY MEMBERS OF THE T CELL LINEAGE.

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J Immunol; 128(4):1718-1722 1982

The SC-1 antigen, identified by thymus-absorbed rabbit anti-mouse brain antiserum, is present on multipotential stem cells. Its presence on cells of the T lineage has been examined by immunofluorescence, and we have demonstrated that it is also a marker for thymic development. Although it is present on the majority of fetal and neonatal thymocytes, its expression declines rapidly and, as early as 1 mo after birth, adult levels are reached. In normal animals, these do not change during adult life, even in mice destined to develop a T cell leukemia. SC-1 does reappear transiently on cells in the regenerating thymus of sublethally irradiated mice. Although the antigen is not associated with preleukemic changes in the thymus, it is expressed on some cells of all spontaneous T lymphomas, and it is uniformly present on tissue culture lines of cell lymphomas. (Author abstract) (11 Refs)

33. MEMBRANE ASSOCIATED REGULATORY EVENTS OF LYMPHOID DIFFERENTIATION.

Miller HC, Esselman WJ
Dept. Microbiology and Public Health, Michigan State Univ., East Lansing, MI, 48824
The Handbook of Cancer Immunology: Volume 9- Humoral Immunity in Relation to Cancer. Waters H, ed. New York, Garland STPM Press, 289 pp., 1981.

Purified mouse B-lymphocytes were completely saturated with antigen (Ag), in a way resembling the effect of the absence of T-lymphocytes or of overwhelming microbial, neoplastic, or endogenous Ag assault on the host. Under conditions of Ag saturation, Ag-specific precursor B-cells became tolerant and differentiated no further. The primary B-cells 'overloaded' temporarily (24-48 hr), becoming unable to receive T-cell signals for differentiation into plasma cells. Mitogen or Ag stimulation caused T-cells to shed membrane molecules, including Thy-1 active glycolipids (GL). Modulated B-cells seemed to be only temporarily unable to bind the Ag; they reached full responsive potential by the time T help signals were ready, and thus were protected during the early stages of Ag accumulation. The cells of neuroblastomas and lymphomas (probably other tumor types as well) shed surface GL continuously. This continuous Ag saturation caused B-cells of all specificities to remain in the suppressed, unresponsive stage, which would prevent Ab-mediated host immune reactions and favor tumor growth. Further research is needed to elucidate the regulation of normal immune responses and devise methods of overcoming the deregulation of host defenses by tumor products. (87 Refs)

34. IMMUNOREGULATION VIA MODIFIED AMINO GROUPS.

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The Handbook of Cancer Immunology: Volume 7- Immune Function and Dysfunction in Relation to Cancer. Waters H, ed. New York, Garland STPM Press, 372 pp., 1981.

The T-lymphocytes are thought to be the primary mechanism of host defense against tumor growth, although many other cells are involved. Sodium cyanate (NaCNO) blocks antigen recognition by (or the activation of) suppressor T-cells, without apparently affecting the memory cells or the 'homing in' of migrating lymphocytes. NaCNO is specific for the T-cell receptor and does not affect the efferent arc of the immune response. NaCNO is directly toxic to a variety of tumors, selectively inhibiting DNA and protein synthesis. The simultaneous administration of deoxycorticosteroid can cancel the immunosuppressive effects of NaCNO on T-cell helper and cytotoxic killer cells. One major goal of tumor immunotherapy is boosting and steering the aberrant immune response to a pathway leading to the destruction of transformed cells. The success of this treatment depends on the initiation of a tumoricidal immune attack which can kill the tumor before suppressive factors or tumor size can inhibit the immune response. NaCNO may be suitable for such immunotherapeutic protocols. (163 Refs)

VIRUS ASSOCIATED ANTIGENS

35. COMPLEMENT-FIXING ANTIBODY TO EPSTEIN-BARR VIRUS SOLUBLE ANTIGEN IN POPULATIONS AT HIGH AND LOW RISK FOR NASOPHARYNGEAL CARCINOMA.

Levine PH, Ebbesen P, Connelly RR, Das S, Middleton M, Mestre M
NCI, Landow Bldg., ID-12, Bethesda, MD, 20205
Int J Cancer; 29(3):265-268 1982

Greenland Eskimos comprise an ethnic group with one of the highest recorded incidence rates for nasopharyngeal carcinoma in the world. Sera from 625 Eskimos and 73 Danes (Caucasians) living in Greenland, as well as from 62 Danes living in Denmark, were tested for complement-fixing antibody to Epstein-Barr virus (EBV) soluble antigen and, from this study group, 129 donors were matched by age and sex for a study comparing antibody to viral capsid antigen, early antigen, and soluble antigen. Both Eskimos and Danes living in Greenland had significantly higher titers of EBV antibodies than Danes living in Denmark, suggesting that environment was more important than genetics or socioeconomic factors in determining the antibody response to EBV. Age and sex were also factors, higher titers occurring in females and young Eskimos. (Author abstract) (21 Refs)

36. EXPRESSION OF HERPES SIMPLEX VIRUS TYPE-COMMON SURFACE ANTIGENS IN CLONAL CELLS OF AN HSV TYPE 2-TRANSFORMED LINE: EFFECT OF ADRIAMYCIN.

Kako D, Ohnishi Y, Kimura S
Dept. Periodontology and Endodontology, Sch. Dentistry, Tokushima Univ., Tokushima 770, Japan
Microbiol Immunol; 25(12):1265-1278 1981

The expression of herpes simplex virus (HSV) type-common surface antigen (CSA) w as studied in a representative cell clone (155-4-03) of hamster cell line 155-4 transformed by HSV type 2. HSV-CSA was detected by the indirect immunofluorescence test. Expression of HSV-CSA was enhanced by treatment with inhibitors of RNA synthesis (adriamycin [ADM] and daunomycin) but not by inhibitors of DNA synthesis (2-iododeoxyuridine, bleomycin, mitomycin C and cytosine arabinoside), even though all of these agents decreased the number of viable cells in culture to about the same extent. Addition of puromycin or 2-deoxy-D-glucose to ADM markedly suppressed expression of CSA, indicating that both protein synthesis and glycosylation are necessary. ADM enhanced expression of CSA was sensitive to protease inhibitors (antipain and p-nitrophenyl-p'-guanidinobenzoate) and procaine. Procaine affects the organization of the cytoskeletal system (microfilaments and microtubules) in animal cells and also inhibits trypsin. Low concentrations of ADM (0.1 ug/ml) and actinomycin D (0.5 ug/ml) increased CSA expression in an additive manner, while optimal concentrations of each (0.25 and 2.0 ug/ml, respectively) did not. These findings indicate that the two drugs enhance CSA expression in the clone by a common mechanism. (40 Refs)

37. PROPAGATION OF HUMAN HEPATITIS A VIRUS IN CELL LINES OF PRIMARY HUMAN HEPATOCELLULAR CARCINOMAS.

Deinhardt F, Scheid R, Gauss-Muller V, Frosner G, Siegl G
Pettenkofer Inst., Pettenkoferstrasse 9a, D-8000 Munich 2, W. Germany
Prog Med Virol; 27:109-113 1981

Successful infection of the hepatoma PLC/PRF/5 cell line with hepatitis A virus (HAV) and detection of HAAg and HBsAg antigens by radioimmunoassay and immunofluorescence are described. HAV also multiplied in HEP 3 B 2.17 cells but could not be grown in HBV-negative Malavu cells. HAV has uncharacteristically slow growth for a supposed enterovirus and has other unique characteristics which may make commercial vaccine production difficult. (11 Refs)

38. DETECTION OF HEPATITIS B VIRUS ANTIGENS IN HEPATOCELLULAR CARCINOMA TISSUES.

Goudeau A, Maupas P, Coursaget P, Drucker J, Chiron JP, Denis F, Diop Mar I, N'Diaye PD
(c/o Maupas) Institut de Virologie, Facultes de Medecine et de Pharmacie, 2 bis, boulevard Tonnelle, F-37000 Tours, France
Prog Med Virol; 27:77-87 1981

A serological and pathological immunofluorescence study of hepatitis B (HBV) antigens was conducted on liver tissues obtained from 15 patients who died from primary hepatocellular carcinoma (PHC) in Dakar, Senegal, where PHC is obvious upon clinical examination and prevalent in patients in the 30-40 yr age range. Tissue localization of hepatitis B surface antigen and hepatitis B core antigen suggested the following etiological scheme for the HBV role in the genesis of PHC: hepatitis with inflammatory phenomena and necrosis followed by post-necrosis cirrhosis with fibrosis and voluminous regenerative nodules; and PHC evolving from the post-necrotic regenerative nodules. (20 Refs)

39. LOCALIZATION OF HEPATITIS B VIRUS ANTIGENS IN HEPATOCELLULAR CARCINOMA.

Nazarewicz-de Mezer T, Slusarczyk J, Krawczynski K, Nowoslawski A

Dept. Immunopathology, Natl. Inst. Hygiene, ul. Chocimska 24, 00-791 Warsaw, Poland

Prog Med Virol; 27:66-76 1981

Studies on the localization of hepatitis B (HBV) antigens by immunofluorescence or immunoperoxidase staining or by fluorochrome- or enzyme-labeled antibodies in cells of patients with hepatocellular carcinoma (HCC) are reviewed. All data obtained by immunomorphological analysis of HCC tissue and indicative of a decreasing potential of expression of HBV antigen with increasing malignancy are compatible with the hypothesis on the oncogenic properties of HBV. (50 Refs)

40. HEPATITIS B VIRAL MARKERS IN PATIENTS WITH CHRONIC HEPATITIS AND WITH PRIMARY HEPATOCELLULAR CARCINOMA IN TAIWAN.

Tong MJ, Chien MC, Lo KJ, Tsai YT, Lee JK

Liver Diagnostic Center, Huntington Memorial Hosp., 100 Congress St., Pasadena, CA, 91105

Prog Med Virol; 27:60-65 1981

Three prospective studies on the relationship between hepatitis B viral markers and primary hepatocellular carcinoma (PHC) were conducted with patients of Chinese origin at two veterans hospitals. The frequencies of hepatitis B surface antigen (HBsAg) and anti-HBs were determined in 94 chronic hepatitis patients, and the patients' progress was followed for 3 yr. Hepatitis B viral markers were measured by radioimmunoassay in a study involving 102 patients with PHC and HBsAg and anti-HBs were determined in patients with acute viral hepatitis (40), chronic hepatitis (161), and PHC (126). (6 Refs)

41. HEPATITIS B INFECTION IN ALCOHOLIC LIVER DISEASE AND PRIMARY HEPATOCELLULAR CARCINOMA IN FRANCE.

Goudeau A, Maupas P, Dubois F, Coursaget P, Bougnoux P

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Prog Med Virol; 27:26-34 1981

The prevalence of hepatitis B virus (HBV) markers was studied in 125 asymptomatic heavy drinkers, 163 patients with alcoholic cirrhosis, and 46 patients with histologically proven primary hepatocellular carcinoma. Hepatitis B surface antigen, anti-hepatitis B surface antigen, and anti-hepatitis B core antigen were tested by solid phase radioimmunoassay. Percentages of HBV markers in the three groups were, respectively, 31.2, 54.6, and 21.7, compared to 5% in a control group of 10,000 normal blood donors from the same area in France. (24 Refs)

42. HEPATIC CANCER AND NON-A NON-B TYPE HEPATITIS.

Shibasaki K, Soga K, Honma A, Ichida F
Dept. Internal Medicine, Nippon Dental Coll. Niigata Dental Sch., Niigata, Japan
Nippon Rinsho; 39(10):3251-3256 1981

Patients with chronic hepatic disease included two groups according to presence or absence of hepatitis B surface (HBs) antigen. Hepatic cancer patients with continuous infection of hepatitis B virus (HBV) were classified B-type hepatocarcinoma, and those with non-A non-B (NANB)-type hepatitis were classified NANB type hepatic cancer. Characteristics of the groups were compared. HBs antigens were detected with the aid of RPHA method in 63/125 patients with chronic hepatitis, 33/129 with cirrhosis, and 57/114 with hepatic cancer. Examination of HBV related antigens and antibodies in the serum of 101 patients with hepatic cancer showed that 60/101 had continuous HBV infection, 31/101 had temporary HBV infection, and 10/101 had no detectable HBV antigens or antibodies. Studies of 129 patients with cirrhotic changes indicated that a higher rate of the patients with HBs antigens developed primary hepatic cancer than did those without HBs antigens. Other studies indicated that hepatic cancer occurred within a shorter period of time in patients with presence of HBs antigen than in those without HBs antigen. Comparison of characteristics of B-type hepatocarcinoma patients (B Group) and NANB-type hepatocarcinoma patients (NANB Group) showed that the B Group patients developed cancer with an average of 5 yr earlier than the NANB Group patients, the male:female ratio of the B Group was less than that of the NANB Group, more NANB Group patients had a history of blood transfusions and hepatitis, and more B Group patients had no history of alcohol consumption. (29 Refs) (In JPN)

43. ADENOVIRUS E1B-58KD TUMOR ANTIGEN AND SV40 LARGE TUMOR ANTIGEN ARE PHYSICALLY ASSOCIATED WITH THE SAME 54 KD CELLULAR PROTEIN IN TRANSFORMED CELLS.

Sarnow P, Ho YS, Williams J, Levine AJ
State Univ. New York, Stony Brook, NY, 11794
Cell; 28(2):387-394 1982

The adenovirus E1b-58kd tumor antigen has been detected in a physical association with a 54 kilodalton cellular protein in adenovirus-transformed mouse cells. Antibody specific for the E1b-58kd protein coimmunoprecipitates a 54 kd protein from transformed, but not from productively infected, cells. Monoclonal antibody specific for the cellular 54 kd protein coimmunoprecipitates the adenovirus E1b-58kd protein from transformed cell extracts. The same or closely related cellular 54 kd protein, associated with the adenovirus E1b-58kd protein, was present in the SV40 large T antigen-54 kd complex previously detected in SV40-transformed mouse cells. The identity of the 54 kd protein is based on the immunological specificities of the anti-54 kd monoclonal antibodies and partial peptide maps of the 54 kd protein associated with the adenovirus and SV40 tumor antigens. The adenovirus E1b-58kd-54 kd complex, like the SV40 large T antigen-54 kd complex, is heterogeneous in size or mass. While all of the cellular 54 kd protein in the adenovirus-transformed cell extract is found in a complex with the E1b-58kd protein, some of the viral 58 kd antigen is detected in a form not associated with the 54 kd protein. The fact that the adenovirus and SV40 tumor antigens, both required for transformation, can be found in physical association with the same cellular protein in a transformed cell is a good indication that these two diverse viral proteins share some common mechanisms or functions. (Author abstract) (43 Refs)

44. SIMIAN VIRUS 40 LARGE TUMOR ANTIGEN: A 'RNA BINDING PROTEIN'?

Khandjian EW, Loche M, Darlix JL, Cramer R, Turler H, Weil R
Dept. Molecular Biology, Univ. Geneva, 1211 Geneva, Switzerland
Proc Natl Acad Sci USA; 79(4,part1):1139-1143 1982

Simian virus 40 large tumor antigen was isolated by immunoaffinity chromatography from monkey or mouse cell cultures undergoing lytic or transforming infection. RNase-treated gel-purified large tumor antigen, on hydrolysis with alkali, gave about equimolar amounts of AMP, CMP, and UMP. Furthermore, RNA fragments of approx 45 nucleotides could be isolated from large tumor antigen purified by the same procedure. Mapping of the T1 oligonucleotides showed a high complexity, as indicated by the presence of unique sequences of 15-30 nucleotides and of poly(A). This is compatible with the hypothesis that these RNA fragments are derived from cellular pre-mRNAs or mRNAs. Our results suggest that Simian virus 40 large tumor antigen is a RNA-binding protein and might possibly be involved in regulation of synthesis, maturation, or translation of cellular mRNAs. (Author abstract) (39 Refs)

45. MONOCLONAL ANTIBODIES AGAINST POLYOMA VIRUS TUMOR ANTIGENS.

Dilworth SM, Griffin BE
Imperial Cancer Res. Fund, Lincoln's Inn Fields, P. O. Box 123, London WC2A 3PX, England
Proc Natl Acad Sci USA; 79(4,part1):1059-1063 1982

A method is described for the production of hybridoma cell lines secreting antibodies directed against the polyoma virus tumor antigens (T-Ags). Ten cloned lines have been established by this procedure and designated alphaPy C1 and C4, with activities against all three T-Ags; alphaPy LT1,-4, and-7, with activities against large T-Ag only; and alphaPy MT5,-7,-10,-13, and-16, with activities against middle T-Ag only. Some of the antibodies appear to react also with specific cellular proteins. Data from studies on alphaPy MT7 point to the possible existence of more than one antigenic form of the viral middle T-Ag and, similarly, from studies on alphaPy LT7, to more than one form of large T-Ag. The approx positions on the polyoma virus genome of the sequences encoding antigenic determinants have been mapped by using defined polyoma virus deletion mutants. The availability of these monoclonal antibodies allows the isolation of large amounts of viral T-Ags. (Author abstract) (30 Refs)

46. IMMUNE SELECTION OF TUMOR CELL VARIANTS IN CHICKENS BEARING TUMORS INDUCED BY AVIAN SARCOMA VIRUS.

Wainberg MA, Israel E, Yu M
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Cancer Res; 42(5):1669-1675 1982

We have compared avian sarcoma cells, cultured from tumors at various stages of growth, in terms of their ability to synthesize infectious progeny virus and to express antigens that are reactive with the sensitized lymphocytes of tumor-bearing host. Cell-mediated immunity in chickens bearing tumors induced by avian sarcoma viruses was monitored by each of a target cell cytotoxicity test and an antigen-driven lymphocyte stimulation assay. Our results show that it is only those tumor cells which have been derived from progressively growing neoplasms that are able to synthesize infectious progeny virus and to specifically interact with the sensitized lymphocytes of tumor-bearing hosts. In contrast, cells from regressing tumors do not express relevant antigens to the same extent as do progressors, and they synthesize noninfectious particles only. Experiments on cellular outgrowths, derived from the plating at limited dilution of progressively growing tumor cells, revealed that such producers of defective virus are present at the earliest stages of tumor growth. Both these cells and regressing tumor cells are poorly stained (about 10%) in indirect immunofluorescence tests by antiserum against viral envelope glycoprotein, whereas tumor cell from progressing neoplasms react well (about 60 to 85%). These results suggest that tumor cells which are found in regressing neoplasms are selected out by a functional immune response directed against cells which are efficient producers of progeny virus. (Author abstract) (24 Refs)

47. PROTEINS ANTIGENICALLY RELATED TO THE HUMAN ERYTHROCYTE GLUCOSE TRANSPORTER IN NORMAL AND ROUS SARCOMA VIRUS-TRANSFORMED CHICKEN EMBRYO FIBROBLASTS.

Salter DW, Baldwin SA, Lienhard GE, Weber MJ
Dept. Microbiology and Public Health, Michigan State Univ., East Lansing, MI, 48823
Proc Natl Acad Sci USA; 79(5):1540-1544 1982

Antibody raised against the purified human erythrocyte glucose transporter specifically precipitated four proteins from normal and Rous sarcoma virus-transformed chicken embryo cells: a major protein of Mr 41,000 and minor proteins of Mr 68,000, 73,000, and 82,000. The Mr 41,000 and 82,000 proteins were found only in a membrane fraction, not in the soluble fraction, and displayed a heterogeneous mobility on NaDodSO4/polyacrylamide gel electrophoresis, suggesting glycosylation. The Mr 41,000 and 82,000 proteins were increased in amount after malignant transformation in direct proportion to the increase in hexose transport rate, and the increase was dependent on the expression of the src gene product, as revealed with a temperature-conditional src mutant. We suggest that the Mr 41,000 and 82,000 proteins are the glucose transporter of chicken embryo fibroblasts, or a component of the glucose transporter. These experiments provide direct evidence that malignant transformation increases the rate of glucose transport by increasing the number of transporters in the membrane. (Author abstract) (27 Refs)

TUMOR ASSOCIATED TRANSPLANTATION ANTIGENS

48. IMMUNOLOGICAL SURVEILLANCE AND CANCER.

Stutman O
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
The Handbook of Cancer Immunology: Volume 7- Immune Function and Dysfunction in Relation to Cancer. Waters H, ed. New York, Garland STPM Press, 372 pp., 1981.

Analysis of the available evidence on the effects of experimental or clinical immunodeficiency on cancer incidence shows that the orthodox immunosurveillance theory (ie, mediated by a thymus-dependent effector cell system capable of destroying nascent tumors) is wrong. The incidence of most tumors is not increased in thymus-dependent immune deficiencies. Immunosurveillance of a 'nonadaptive' nature may be involved. Macrophages and the non-macrophage natural killer (NK) and natural cytotoxic (NC) cells, which are cytotoxic to tumor cells without specific preimmunization, may be involved in surveillance mechanisms in vivo. These responses may act as putative surveillance devices against non-antigenic tumors, although they are probably not directed against conventional tumor-associated antigens. The fact that most clinical tumors seem to be monoclonal argues against a highly efficient surveillance by either the macrophages or the NK-NC cell system. Procedures interfering with or potentiating macrophage or natural cell-mediated cytotoxicity may provide additional evidence of the efficiency (even the existence) of these in vivo defenses against tumors. Experimental or clinical models of selective deficiencies of macrophage or cell-mediated cytotoxicity may provide additional information. Future research should probably involve experiments designed to determine whether or not immunologic surveillance is mediated by some other mechanism(s). (136 Refs)

49. RETARDATION AND PROMOTION OF GROWTH OF SPONTANEOUSLY APPEARING TUMORS USING IMMUNE LYMPHOCYTES PREVIOUSLY EXPOSED TO EMBRYONIC ANTIGENS.

Gorczynski RM, MacRae S
Ontario Cancer Inst., Toronto M4X 1K9, Ontario, Canada
Cancer Res; 42(3):784-790 1982

Spleen lymphocytes taken from mice at various stages of pregnancy or growth of sc syngeneic tumor implants have been examined for their ability to cause cytolysis of embryo fibroblasts in culture or to affect the growth of the transplanted tumor cells in vivo. Activity of different lymphoid populations in affecting tumor growth in vivo was correlated with activity in vitro, whether cytolysis (growth inhibition) or blocking of cytolysis (growth promotion) was considered. The evidence favors an important role for lymphoid responses to embryo-associated antigens in the control of spontaneous tumor growth, although one cannot yet rule out a crucial role for the host milieu rather than, or in addition to, host cellular elements being the important feature of this control process. (Author abstract) (29 Refs)

50. IMMUNOTHERAPEUTIC EFFECTS OF TUMOR-SPECIFIC TRANSPLANTATION ANTIGENS RELEASED BY 1-BUTANOL.

Kahan BD, Pellis NR, LeGrue SJ, Tanaka T
Dept. Surgery, Div. Immunology and Organ Transplantation, Univ. Texas Medical Sch., 6431 Fannin St., Houston, TX, 77030
Cancer; 49(6):1168-1173 1982

Active immunotherapy with materials extracted from a murine methylcholanthrene-induced sarcoma using single phase solutions of 2.5% 1-butanol evoked host resistance against supralethal burdens of neoplastic cells deposited subcutaneously or delivered hematogenously. After curative resection of progressing 1 cm tumors, postsurgical immunity against subsequent subcutaneous neoplastic challenges was potentiated by weekly injections of crude butanol extracts. In a conventional therapy model, hosts bearing progressing 4 mm subcutaneous tumors displayed neoplastic regression following chemoimmunotherapy with cyclophosphamide and tumor extracts. Therapeutic effects were demonstrated not only against subcutaneous neoplasms, but also against hematogenously disseminated pulmonary and extrapulmonary metastases introduced by intravenous inoculation of sarcoma cells. These findings suggest that tumor extracts may afford potent therapeutic adjuvant for patients bearing a small body tumor burden but at high risk of disease recurrence. (Author abstract) (21 Refs)

CLINICAL DIAGNOSTIC STUDIES

51. IMMUNOSUPPRESSION IN NEOPLASIA.

Anderson WL, Tomasi TB
Mayo Medical Sch., Rochester, MN, 55901
The Handbook of Cancer Immunology: Volume 7- Immune Function and Dysfunction in Relation to Cancer. Waters H, ed. New York, Garland STPM Press, 372 pp., 1981.

An immunologic challenge elicits the formation of cells and factors which both enhance and suppress (or terminate) the immune reaction. The net result of the challenge depends on the ratios of these enhancing and inhibitory signals. There is evidence for an association between immunosuppression and neoplasms, but it is not clear whether the immunosuppression is required for tumor establishment (or tumor growth) or a secondary event. Some soluble immunosuppressive factors have been isolated from sera and tumors, but more evidence is needed as to their natures and activities. The possibility that a virus may be responsible for the activity of suppressor cells has not always been excluded. Antigen-specific suppressor T cells are clearly involved in the establishment of tumors. The role of nonspecific suppressor cells is less clear, especially in view of the finding that tumor-bearing animals with elevated levels of nonspecific suppressor cells are not always immunologically comprised. A good correlation has been established between anergy and the presence of soluble immunosuppressive factors (not yet purified) in cancer patients. However, immunosuppression has not been discovered in all or even most cancer patients, and 33% of all cancer patients do not show elevated levels of the immunosuppressive factors which can now be analyzed. These findings suggest that immunosuppression is not a general phenomenon in human cancer and therefore not a requirement for tumor development. However, it is possible that immunosuppressive elements may act locally at the tumor site. Currently used tests of immune function may not detect subtle but important abnormalities. Future research should provide both a better understanding of both immune regulation in neoplasia and normal immune homeostatic mechanisms. (124 Refs)

52. CLINICAL AND HISTOPATHOLOGICAL STUDY OF NASAL T CELL LYMPHOMA.

Yamanaka N
Dept. Otolaryngology, Sapporo Medical Coll., Sapporo, Japan
Jibi Inkoka; 53(12):1075-1086 1981

Clinical and histopathological features of two cases with nasal T cell lymphoma in which an initial clinical diagnosis of 'rhinitis gangrenosa progressiva' or lethal midline granuloma was made. The histopathological examinations of their autopsy specimens proved that their nasological disease could all be identified to be malignant lymphoma arising from the nasal cavity, which showed, in general, histopathological characteristics described for T cell lymphoma derived from peripheral T cells. This histopathological observation was then confirmed by immunofluorescence studies using various antisera directing to either human T or B cell surface antigens, which clearly demonstrated that their malignant cells bore human T cell antigens but lacked human Ia-like antigens as well as surface immunoglobulins, indicating their peripheral T cell origin. These data may suggest that so-called 'rhintis gangrenosa progressiva' or lethal midline granuloma contains at least two distinct disease categories, one of which is Wegener's granulomatosis, and another of which is nasal T cell lymphoma described herein. (Author abstract) (25 Refs) (In JPN)

53. LYMPH NODE T CELLS IN HODGKIN'S DISEASE: ANALYSIS OF SUSPENSIONS WITH MONOCLONAL ANTIBODY AND ROSETTING TECHNIQUES.

Aisenberg AC, Wilkes BM
Huntington Lab., Massachusetts General Hosp., Boston, MA, 02114
Blood; 59(3):522-527 1982

Suspensions prepared from lymph nodes involved by Hodgkin's disease and from a diverse group of lymph node hyperplasias were investigated with a panel of 10 monoclonal antibodies and a variety of conventional surface marker techniques. In both Hodgkin's disease and hyperplasia, 60%-70% of the cells were T lymphocytes, approximately 80% of the inducer/helper subset and 20% of the cytotoxic/suppressor subset. The most prominent differences observed between Hodgkin's disease and hyperplastic T cells are explained by greater affinity of the sheep cell receptor on the surface of the lymphoma T lymphocytes. This greater affinity was best demonstrated by the formation of rosettes with unsensitized or immunoglobulin-sensitized sheep erythrocytes after incubation at 37 C, an occurrence observed only with Hodgkin's disease cells. In addition, in hyperplasia, a variable proportion of lymphocytes reacting with the anti-T-cell monoclonal antiserum OKT3 failed to form unsensitized rosettes at 4 C (E rosettes), while in Hodgkin's disease there was near equivalence of T cells that reacted with the antiserum and formed E rosettes. In addition to the increased infinity for sheep erythrocytes, some Hodgkin's disease specimens displayed increased reactivity with the monoclonal antibody OKM1, which detects monocytes and granulocytes, and the monoclonal antibody OKT10, which reacts with early thymocytes. Finally, 14 of 20 lymphoma samples exhibited polar migration of the fluorescent material (capping) with one or more antisera (most frequently OKI1, the monoclonal antibody with specificity for the Ia-like antigen). These findings are useful in distinguishing Hodgkin's disease lymph nodes from hyperplasia by surface marker characteristics and may be relevant to older observations that Hodgkin's disease T cells aggregate about Reed-Sternberg cells. (Author abstract) (26 Refs)

54. ELECTRON MICROSCOPIC IDENTIFICATION OF LANGERHANS CELLS IN THE DERMAL INFILTRATES OF MYCOSIS FUNGOIDES.

Jimbow K, Chiba M, Horikoshi T
Dept. Dermatology, Sapporo Medical Coll., Minami 1, Nishi 16, Sapporo 060, Japan
J Invest Dermatol; 78(2):102-107 1982

The importance of the physical interaction between epidermal Langerhans cells and malignant cells in mycosis fungoides (MF) has been stressed recently. To further evaluate the concept, electron microscopic study was carried out to identify whether or not Langerhans cells are also present in the dermal infiltrates of MF. The cells with characteristic Langerhans cell-granules were found in the dermal infiltrates, from early patch to tumor lesions of MF. No vacuolous change suggestive of cell degeneration was found in these cells. These Langerhans cells revealed only a small number of specific granules and nuclear cleavage and chromatin pattern similar to those of malignant lymphoid cells, thus hardly differentiating two cell types in a low power view. Similar to epidermal MF lesions, however, a close apposition of dermal Langerhans cells with malignant lymphoid cells was seen. On one occasion, one Langerhans cell was present at the epidermodermal junction, appearing as being in the process of crossing over the basal lamina. Inasmuch as malignant cells in MF have been shown to possess the functional properties of helper T cells and receptors for Ia (immune associated antigen), expressed in the epidermis solely on Langerhans cells, our findings may further suggest that these malignant T cells bind to Langerhans cells through a 'lock and key' mechanism involving membrane-bound Ia. (Author abstract) (23 Refs)

55. PHENOTYPE CHARACTERIZATION OF CHRONIC LYMPHOCYTIC LEUKEMIA WITH MONOCLONAL ANTIBODIES AND SURFACE RECEPTORS.

Estevez ME, Sen L, Diez RA, Bellouard A, Santos I
Departamento de Microbiologia, Instituto de Investigaciones, Hematologicas Academia Nacional de Medicina, Buenos Aires, Argentina
Medicina (B Aires); 41(Suppl):123-130 1981

Different immunologic and enzymatic techniques as well as monoclonal antibodies (MA) were used in 33 patients (21 men, 12 women; 42-84 yr old) with chronic lymphocytic leukemia. Analyses were performed when WBC was greater than 10,000/mm square. T cell markers were determined with sheep red blood cell rosette test (E4 and E37). B cell markers were determined using mouse red blood cell rosette formation test (ER). C3 serum complement was determined by erythrocyte antibody complement (EAC) rosette test. Cell surface (sIg) and cytoplasmic (cIg) immunoglobulins were determined by immunofluorescence. Surface antigens T1, T3, T4, T6, T8, T9, T10, T11a, Ia1, and M1 were evaluated with MA of OK series. All the patients had phenotype B and were divided into four groups (early immature, immature, mature, and very mature). EAC was present in all the patients, and only 1/3 had ER values greater than 20%. Range of values was 0-37% for E4, 0-27% for E37, 22-94% for EAC, and 0-82% for ER. Results of monoclonal antibodies were positive in 11/12 patients for Ia1, in 7/12 for T1, and in 2/12 for T10, all the others were negative. (16 Refs) (In SPA)

56. MONOCLONAL ANTIBODY AGAINST A MEMBRANE ANTIGEN CHARACTERIZING LEUKEMIC HUMAN B-LYMPHOCYTES.

Forster HK, Gudat FG, Girard MF, Albrecht R, Schmidt J, Ludwig C, Obrecht JP
Pharma Res. Div., F. Hoffmann-La Roche and Co., Ltd., Basel, Switzerland
Cancer Res; 42(5):1927-1934 1982

In the diagnosis of non-Hodgkin's lymphomas, the ready characterization of the neoplastic cell lineage by analysis of cell surface markers is of great importance. We present evidence for the existence of a human B-leukemia-associated antigen recognized by a complement-fixing monoclonal antibody (anti-Y 29/55). A hybridoma was produced by fusing mouse myeloma cells and splenocytes of a mouse immunized against lymphoid cells of a patient with B-cell chronic lymphocytic leukemia. Characterization of anti-Y 29/55-reactive normal and malignant leukocytes was demonstrated by cytolysis and indirect immunofluorescence. This revealed reactivity with an antigen on B-lymphoma cells (11 patients), on leukemic lymphocytes in B-cell chronic lymphocytic leukemia (13 patients), and on malignant cells in hairy-cell leukemia (2 patients) but not on leukemic cells of T-cell acute lymphoblastic leukemia (1 patient), on T-lymphoma cells (1 patient), on cells of acute myeloblastic leukemia (4 patients), or of chronic myeloid leukemia (4 patients). No specific cytolysis occurred with B- and T-peripheral blood lymphocytes from (a) healthy donors (16 individuals), (b) patient with reactive lymphocytosis (1 patient), (c) nonleukemic multiple myeloma (6 patients), or (d) Hodgkin's disease (3 patients). Surface immunoglobulin-positive, sheep RBC-negative lymphocytes isolated from human spleen (3 individuals), tonsils (7 individuals), and lymph nodes (1 individual), however, we recognized. It is concluded that leukemic B-cells carry a marker characteristic of nonrecirculating sessile B-lymphocytes. (Author abstract) (54 Refs)

57. LYMPHOCYTIC LYMPHOMA AND SYSTEMIC LUPUS ERYTHEMATOSUS. THEIR COEXISTENCE WITH ANTIBODY TO THE SM ANTIGEN.

McCarty GA, Rice JR, Fetter BF, Pisetsky DS
Div. Rheumatic and Genetic Diseases, Dept. Medicine, Duke Univ. Medical Center, P.O. Box 3905, Durham, NC, 27710
Arch Pathol Lab Med; 106(4):196-199 1982

The serologic and clinical features of a 32-yr-old woman with coexistent systemic lupus erythematosus and lymphoma were studied. A cervical node biopsy specimen demonstrated nodular, poorly differentiated lymphocytic lymphoma; subsequent development of polyarthralgias prompted evaluation for connective-tissue disease, and a high titer of antinuclear antibody was found. Immunochemical studies proved that this antibody was directed to the Sm antigen, a serologic finding highly specific for systemic lupus erythematosus. The antibody has been maintained throughout the course of the patient's disease, characterized by persistent lymphadenopathy, pleuropericarditis, arthritis, hypocomplementemia, hyperglobulinemia, and a slight elevation of titers of anti-DNA antibody. The course of the lymphoproliferative disorder has been consistent with that of an indolent non-Hodgkin's lymphoma. In sera from other patients with lymphoproliferative disorders, anti-Sm antibody was not found. These findings emphasize the importance of establishing the antigenic specificity of antinuclear antibodies detected in the sera of patients with neoplasia. (Author abstract) (43 Refs)

58. NON-T, NON-B LYMPHOMAS ARE RARE IN CHILDHOOD AND ASSOCIATED WITH CUTANEOUS TUMOR.

Bernard A, Murphy SB, Melvin S, Bowman WP, Caillaud J, Lemerle J, Boumsell L
Laboratoire d'Immunologie des Tumeurs de l'Enfant, Institut Gustave-Roussy, 9480 0 Villejuif, France
Blood; 59(3):549-554 1982

Tumor cells from a total of 116 children with non-Hodgkin's lymphoma were studied for their pattern of reactivity with a battery of cell markers, including their capacity for spontaneous formation of sheep erythrocyte rosettes (E-rosettes), demonstration of surface immunoglobulins (SIg), and positivity with antisera against T-cell antigens, the common acute-lymphoblastic-leukemia-associated antigen (cALLa), and Ia-like antigens. Fifty-eight children (50%) had T-cell lymphomas, including all those with mediastinal tumors. Fifty children (43%) had B-cell lymphomas, including 44 of the 45 with abdominal primaries. Eight children (7%) non-T, non-B tumors, four of whom presented at a young age with cutaneous lymphoblastic tumors. These results demonstrate that the great majority of children with NHL, not leukemic at diagnosis, have tumors clearly committed to either T- or B-cell differentiation pathways and only rarely exhibit the common ALL phenotype (cALLa+, Ia+, E-, T-, SIg-), contrasting with the distribution of childhood lymphoblastic leukemias. The unusual association of these non-T, non-B cases with skin involvement has not previously been reported, raising speculation regarding patterns of lymphocyte traffic and origins of childhood lymphomas and leukemias. (Author abstract) (32 Refs)

59. USE OF ANTISERA TO EPITHELIAL MEMBRANE ANTIGEN FOR THE CYTODIAGNOSIS OF MALIGNANCY IN SEROUS EFFUSIONS.

To A, Coleman DV, Dearnaley DP, Ormerod MG, Steele K, Neville AM

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J Clin Pathol; 34(12):1326-1332 1981

A new human antigen, designated epithelial membrane antigen (EMA), has recently been described on surface membranes of a wide variety of normal epithelium but not on connective tissue cells. The antigen is only weakly expressed on normal or reactive mesothelium. Increased expression of the antigen has been observed in most neoplasms of epithelial origin and in malignant mesothelioma. We have investigated the possibility of using this difference in the expression of the antigen to distinguish between mesothelial cells and malignant cells in cytological smears of serous effusions. This distinction cannot always be made on morphological grounds alone and problems of differential diagnosis are encountered in about 15% of all specimens of serous effusions sent for cytological examination. Using antisera to EMA we have applied an indirect immunoalkaline phosphatase technique to alcohol-fixed smears prepared from serous effusions and have found that intense staining of the antigen is confined to effusions from patients in whom there is either clinical or cytological evidence of malignancy. The technique proved to be especially useful in cytologically equivocal cases, where there were problems of differential diagnosis. (Author abstract) (11 Refs)

60. INTESTINAL MUCINOUS SUBSTANCES IN GASTRIC INTESTINAL METAPLASIA AND CARCINOMA STUDIED BY IMMUNOFLUORESCENCE.

Ma J, De Boer WG, Nayman J

Clinical Res. Center, Royal Southern Memorial Hosp., P. O. Box 165, Caulfied South, Victoria 3162, Australia

Cancer; 49(8):1664-1667 1982

Immunofluorescent studies using specific antisera against intestinal mucins revealed small intestinal mucin antigen (SIMA) and large intestinal mucin antigen (LIMA) in areas of intestinal metaplasia of the stomach. In 25 gastric carcinomas studied, both these antigens were detected in 7 carcinomas, SIMA only was present in 4 and LIMA only in 4 cases; the antigens could not be detected in 10 of the carcinomas. In 21 of the 25 gastric cancer operation specimens, including the 15 carcinomas positive for intestinal mucin antigens, there was evidence of chronic gastritis and intestinal metaplasia. These immunohistologic observations confirm the results of recent histochemical studies that both small and large intestinal type mucins are present in intestinal metaplasia and gastric carcinomas. Our findings provide further evidence that at least a proportion of gastric carcinomas may supervene on intestinal metaplasia. The absence of one or both antigens in gastric carcinomas may indicate stages of dedifferentiation or alternatively differences in histogenesis. (Author abstract) (10 Refs)

61. THE TENNESSEE ANTIGEN TEST. AN EVALUATION IN CANCER AND NON-CANCER PATIENTS AND NORMAL SUBJECTS.

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Dept. Medical Oncology, Charing Cross Hosp., Fulham Palace Road, London W6 8RF, England

Br J Cancer; 45(2):223-229 1982

The Tennagen test has been evaluated in 'normal' subjects, patients with cancer (predominantly colorectal) and patients with non-malignant disease. The incidence of positive values was found to be higher in patients with clinically active cancer than in those with benign conditions or normal subjects. In our hands the test fell far short of the 90% reliability previously claimed. This may be partly due to an underestimate of the upper normal limit in earlier studies. A small series of follow-up studies after resection for colorectal cancer have so far failed to reveal any advantage to be gained by Tennagen tests over existing methods, but these studies will be continued. (Author abstract) (10 Refs)

62. IMMUNE REACTIVITY IN COLORECTAL CARCINOMA: CLINICAL VALUE FROM A SURGICAL VIEWPOINT.

Muhrer KH, Schwemmle K, Filler D, Kahle M

Chirurgische Universitatsklinik, Klinikstrasse 29, D-6300 Giessen, W. Germany

Chirurg; 53(2):112-116 1982

Specific immune reactions to colorectal carcinoma (CRC) were studied. NaCl extracts of tumor cell-membrane proteins were made from samples of CRC, gastric cancer (GC), bronchial carcinoma (BC), and mammary carcinoma (MC). CRC types included well, moderately, and poorly differentiated adenocarcinoma. Lymphocytes preparations were made from venous blood of 36 patients with histologically confirmed CRC, 15 patients with precancerous adenoma of the colon, 19 patients with inflammation of the colon, and 54 healthy controls. Reactivity to tumor antigens was measured by inhibition of electrophoretic cell migration using sheep RBC as indicator cells. Inhibition of greater than 5% was considered positive. Positive reactions to CRC extract were obtained with lymphocytes from 31/36 CRC patients. Average inhibition was 12.0 +-7.03% for Duke's Stage A CRC, 11.18 +-5.06% for Stage B, 13.26 +-7.03% for Stage C, and 16.80 +-7.65 % for patients with extensive metastases. Negative results were obtained from 48/56 controls. Positive results were obtained from 10/15 patients with adenoma and 11/19 patients with inflammatory conditions. Of 36 CRC patients, 8 showed positive reactions to GC extracts; none showed positive reactions to BC or MC. Reactivity to allogeneic tumor extracts indicated the sensitivity was specific for the tumor type rather than for the individual. Results indicate specific sensitivity of lymphocytes from CRC patients to CRC antigens and some weak cross-reactivity to antigens from other tumor types. Reliability of the test is limited by positive sensitivity of patients with acute inflammatory conditions. (15 Refs) (In GER)

63. DISTRIBUTION OF ABH ANTIGENS IN TUMORS OF THE BLADDER. A RETROSPECTIVE IMMUNOFLUORESCENCE STUDY.

Rouger P, Vallancien G, Leclerc JP, Gane P, Salmon C
Centre National de Referene pour les Groupes Sanguins, U76, CNTS, INSERM, 53 boulevard Diderot, F 75012 Paris, France
Nouv Presse Med; 11(6):419-421 1982

ABH antigens are normally present on the surface of the healthy urinary epithelium. In a significant number of patients with tumor of the bladder the epithelium loses these antigens. The loss appears to be unrelated to the grade or stage of the tumor, but the prognosis seems to be brighter when the ABH antigens are retained. (Author abstract) (16 Refs) (In FRE)

64. CURRENT CONCEPTS IN CANCER: OVARY - MANAGEMENT OF STAGE I AND II DISEASE. NEW IMMUNOTHERAPEUTIC AND DIAGNOSTIC APPROACHES TO OVARIAN CANCER.

Order SE, Klein JL, Torres JP
Dept. Radiation Oncology, Johns Hopkins Comprehensive Cancer Center, Baltimore, MD, 21205
Int J Radiat Oncol Biol Phys; 8(2):259-261 1982

Dissemination, staging, prognostic factors, and the biological characteristics of the ovarian cancer (OC) cell are evaluated according to the aspects of new immunotherapeutic and diagnostic approaches to OC. Clinical OC which migrates through the diaphragmatic lymphatics and into general circulation, does not yield the expected number of disseminated metastases that occur with other cancers. Evaluation of the peritoneal cavity for biomarkers in establishing diagnosis and in determining tumor cell persistence after treatment are possibilities for future clinical programs. The use of immuno-specific antibody will also probably find a role in actual therapy. Alpha and beta globulins associated with OC have been identified. Tumor associated antigens (TAA) are normal tissue proteins increased in concentration as a result of cancer. TAA may be bound by antibody at tumor sites even if the antigen is present in other normal tissues. Exposing the TAA first to tumor, allows for tumor binding prior to potential binding in other sites bearing the same antigen. TAA appear to be in significantly greater concentration than so called tumor specific antigens. Antiserum to TAA when administered ip in an experimental OC was curative. Cure was achieved by inducing macrophage reactivity against tumor cells. Both TAA and tumor specific antibodies may be used as immune direct binding agents, and contribute to increased cure rate. (20 Refs)

OTHER RELATED STUDIES

65. THE HANDBOOK OF CANCER IMMUNOLOGY, VOLUME 7. IMMUNE FUNCTION AND DYSFUNCTION IN RELATION TO CANCER.

Waters H
NIH, Bethesda, MD
The Handbook of Cancer Immunology, Volume 7. Immune Function and Dysfunction in Relation to Cancer. New York, Garland STPM Press, 372 pp., 1981.

Aspects of immune function and dysfunction as they relate to cancer are presented. Immunological surveillance is discussed with consideration of the thymus, macrophages, cytotoxic cells, and immunodepression in cancer patients. Immune responses to challenge, including cellular and humoral factors, and the role of these factors in immune suppression are considered. Other topics include regulation of immune response, immunobiology of chemotaxis and metastases, and the role of macrophages and other cells in carcinogenesis. Macrophage arginase and arginine consumption are related to tumor growth. Also discussed are rejection and enhancement of grafts, the role of antigens and antibodies in idiotype regulation and T-lymphocyte modulation, immunoregulation via modified amino groups, immunity and tolerance to transplantation antigens, and production of specific unresponsiveness to tissue allografts by immunosuppression and donor antigen. Normal and abnormal conditions, as well as intermediate conditions are compared. Discussion of topics includes review, original findings, and speculation about future investigative efforts. (1420 Refs)

66. EPIDEMIOLOGIC CHARACTERISTICS OF CHILDHOOD CANCER.

Austin DF, Nelson VE, Johnson LF
Resource for Cancer Epidemiology, Health Services, 1450 Broadway, Oakland, CA, 94612
Front Radiat Ther Oncol; 16:9-17 1982

In the San Francisco metropolitan area, the incidence of malignancies in childhood (0-19 yr old) remained substantially unchanged over a 10-yr period (1969-1978), but the mortality rate declined substantially in all pediatric age groups. The mortality/incidence ratio in all age groups combined declined by about 20% during this time, apparently reflecting improved treatment procedures. These changes have been greater in children 0-14 yr old than in the 15-19 age group. Examination of mean annual age-specific mortality rates for the leukemias suggests that leukemias (especially acute leukemias) of childhood and adulthood may be etiologically different diseases. There responses to treatment suggest that they may be biologically different diseases. Possible etiologic factors for childhood leukemia include prenatal radiation exposure, chromosomal abnormalities, and possibly antigenic stimulation of the WBC population at a critical period of gestation by certain biologic agents. The children of women who had been in the first trimester of pregnancy during an influenza A epidemic showed a 3-4-fold increase in the risk of childhood leukemia. Investigations of childhood leukemia clusters have almost uniformly been inconclusive. A cluster of Ewing's sarcoma (30 recorded cases over an 8-yr period; 20% of the entire 8-yr incidence) has been discovered in one small community (within a 30-block diameter) in the San Francisco area. It is hoped that investigations of such clusters may provide clues for the prevention of the disease. (6 Refs)

67. IMMUNOTOXINS: HYBRID MOLECULES COMBINING HIGH SPECIFICITY AND POTENT CYTOTOXICITY.

Jansen FK, Blythman HE, Carriere D, Casellas P, Gros O, Gros P, Laurent JC, Paolucci F, Pau B, Poncelet P, Richer G, Vidal H, Voisin GA
Centre de Recherches Clin-Midy, 34082 Montpellier, France
Immunol Rev; 62:185-216 1982

Experience with four different immunotoxin (IT) models is used as a basis for review of the high specific activity of conjugates between antibodies and the A-chain of ricin, the essential requirements for optimal in vitro IT activity, and advantages and limitations of IT in vitro and in vivo. The three subunits of IT, the toxin, the antibody, and the chemical linkage, are described. After presentation of the cellular model, in vitro and in vivo IT activities are demonstrated. Some conditions necessary to compare ITs of different origin and the possible applications of IT are listed. In vitro properties (sensitivity of different cell lines to toxin, ultrastructural lesions resulting from ricin activity) and in vivo properties (general toxicity, histopathological alterations) of ricin and ricin A-chains are described. Labile, stable, and long spacer disulfide bridges are considered. Cellular models are described for artificial antigens, and mouse differentiation, human differentiation, and human tumor-associated antigens. Advantages of IT include immunological specificity, high efficiency, potentiation, stability, and reprodu cibility. Essential requirements for high IT efficiency include high purification A-chain, nondenaturing labile disulfide bridge, high affinity of purified antibodies, and potentiation of IT activity. Limitations of IT include relative cellular resistance, slow kinetics, and dependence on in vitro conditions. In vivo findings on IT physiopathology (lethal doses, in vivo half-life, nonspecific toxicity, immunogenicity) and tumor growth inhibition are reported. (55 Refs)

68. ANTIBODY MEDIATED DELIVERY OF TOXIC MOLECULES TO ANTIGEN BEARING TARGET CELLS.

Raso V
Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115
Immunol Rev; 62:93-117 1982

The ability of hybrid antibodies with dual specificity to deliver toxic agents to immunoglobulin (Ig)-bearing target cells is reviewed. Progress on both the Ig and CALLA (conjugates which are selectively cytotoxic for human cells bearing the acute lymphoblastic leukemia antigen) are discussed. Topics discussed include hybrid antibodies with simultaneous cell surface and toxic agent binding activity (anti-neocarzinostatin, anti-human IgG hybrids and anti-ricin A chain/anti-human IgG hybrids) and selectively cytotoxic antibody-ricin A chain conjugates (human Ig directed antigen binding fragment [F(ab')]-A chain conjugate, monoclonal human kappa-chain specific F(ab')2-A chain conjugate, and monoclonal CALLA-specific F(ab')-A chain conjugates). Hybrid-mediated enhancement of toxicity has been achieved using neocarzinostatin, whole ricin, and free ricin A chain. (43 Refs)

69. MONOCLONAL ANTIBODY-RICIN OR RICIN A CHAIN HYBRIDS: KINETIC ANALYSIS OF CELL KILLING FOR TUMOR THERAPY.

Neville DM, Youle RJ
Lab. Neurochemistry, Section on Biophysical Chemistry, Natl. Inst. Mental Health, Bethesda, MD, 20205
Immunol Rev; 62:75-91 1982

Effects of three different types of ricin hybrids (antibody thioether linked to intact ricin, antibody disulfide linked to the ricin A chain, and antibody-S-S-A chain to which the ricin B chain is added as a separate entity) conjugated with monoclonal antibody having affinity for the murine thymic adult differentiation antigen Thy 1 on targeted cells are reviewed in relation to tumor cytotoxicity. Entry mechanisms and data regarding parent toxins are considered. (30 Refs)

70. ANTIBODIES CONJUGATED TO POTENT CYTOTOXINS AS SPECIFIC ANTITUMOR AGENTS.

Moolten FL, Schreiber BM, Zajdel SH
Boston Univ. Sch. Medicine, Boston, MA
Immunol Rev; 62:47-73 1982

The ability of toxins, enzymes, radioisotopes, and cytotoxic drugs linked to antibodies to selectively kill cells bearing surface antigens that are targets for the antibodies is reviewed. Criteria for the complexes include the following: the cytotoxin must be capable of acting after delivery to the cell surface by the antibody, the desired biologic properties of the components must survive the conjugation process, the conjugate must be stable until delivered to its site of action, the specificity of the conjugate must reflect primarily the specificity of the antibody complex, and the toxic moiety must be extraordinarily potent. Conjugates tested for antitumor activity include diphtheria toxin conjugates, Pseudomonas aeruginosa toxin conjugates, ricin conjugates, and phospholipase and ribonuclease conjugates. In vitro, each of the agents, when conjugated to antibodies directed against a variety of cell-surface antigens, was selectively cytotoxic to cells bearing those antigens. In vivo, diphtheria toxin conjugated to antibodies directed against the dinitrophenol (DNP) hapten reduced the incidence and growth rate of tumors in hamsters concurrently inoculated with DNP-coated sarcoma cells. When tested against a more sensitive Simian virus 40-induced tumor, two conjugate preparations induced permanent regressions of established tumor in 20% and 56% of treated hamsters. (65 Refs)

71. IN VITRO AND IN VIVO EFFICACY OF CONJUGATES OF DAUNOMYCIN WITH ANTI-TUMOR ANTIBODIES.

Arnon R, Sela M
Dept. Chemical Immunology, Weizmann Inst. Science, Rehovot 76100, Israel
Immunol Rev; 62:5-27 1982

Studies in vitro and in vivo on daunomycin (DN) conjugates with antibodies to several mouse and rat tumor-selective antigens using both conventional and monoclonal antibodies are summarized. Topics discussed in relation to DNA-antibody conjugates include conjugation (direct binding procedure), linking of DNA via dextran bridge, pharmacological activity of the protein-bound drug, and antibody activity of the conjugates. Other topics discussed include conjugates with antigen binding fragment dimers, in vitro efficacy of conjugates, mode of action of the conjugates (in vitro uptake of DNA conjugates, 'homing' of anti-tumor antibodies and conjugates), in vivo efficacy of the conjugates on murine experimental tumors, and efficacy of conjugates on rat hepatoma. Antibodies may serve as carriers for anti-cancer drugs to tumor cells. (43 Refs)

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IMMUNOBIOLOGY AND CANCER

Tumor-Associated Antigens

SERIES CB05 No. 82/09

SEPTEMBER, 1982

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DETECTION/ CHARACTERIZATION/ ISOLATION

1. ISOLATION AND PARTIAL CHARACTERIZATION OF A NUCLEAR ANTIGEN (68/6.3) FROM THE NAMALWA CELL LINE (A BURKITT LYMPHOMA).

Chan PK, Frakes RL, Busch RK, Busch H
(c/o H. Busch) Dept. Pharmacology, Baylor Coll. Medicine, Houston, TX, 77030
J Cancer Res Clin Oncol; 103(1):7-16 1982

A nuclear antigen was purified from the 0.01 M Tris-HCl/pH 8 extract of nuclei of the Burkitt tumor Namalwa cell line to electrophoretic homogeneity by DEAE cellulose chromatography, affinity chromatography, and preparative isoelectric focusing. The yield of antigens was 0.02% of the nuclear 0.01 M Tris-HCl/pH 8 extract. On two-dimensional gel electrophoresis, the major antigen separated into two adjacent protein spots with mol wt of 68,000 and an approx pI of 6.3 (68/6.3 A and 68/6.3 B). A minor antigen had a mol wt of 61,000 and pI of 6.0 (61/6.0). Fourteen 125I-labeled peptides were obtained from the tryptic digest of the major antigen (68/6.3 A and 68/6.3 B). The amino-acid composition analysis of the purified

HE 20. 3173/2:

antigens indicated that the amino acids in the highest content were glycine (15%), glutamic acid (11.6%), and serine (9%); the ratio of acidic to basic amino acids were 1.95. In studies on nucleolytic activity, the purified antigen produced a single-stranded and then a double-stranded cleavage of PM 2 and pBR 322 DNA. This antigen is the first purified nuclear antigen that reacts with the HeLa-specific nucleolar antibodies. (Author abstract) (28 Refs)

2. A MONOCLONAL ANTIBODY DEFINING A BURKITT LYMPHOMA ASSOCIATED ANTIGEN.

Wiels J, Fellous M, Lenoir G, Tursz T
Laboratoire de Immunologie, Clinique Institut G. Roussy, 94800 Villejuif, France
Protides Biol Fluid Proc Colloq; 29:899-902 1982

Reactivity of monoclonal antibody 38-13, obtained by fusing murine myeloma cells with Lewis rat splenocytes sensitized with Daudi cells (human Burkitt lymphoma), was investigated. Negative results were obtained in all patients with B chronic lymphoid leukemia, acute lymphoid leukemia (T and nonT-nonB), acute myeloid leukemia, acute monoblastic leukemia, Hodgkin's disease, T cell lymphosarcoma, and B cell lymphosarcoma (nodular and diffuse). Positive results were observed in 4/8 patients with B cell Burkitt lymphoma. When the specific reactivity of 38.13 ascites was tested with a panel of cell lines of various origins, both by complement dependent lymphocytotoxicity tests and indirect membrane immunofluorescence assays, all the positive target cells were of Burkitt's lymphoma origin. Negative results were obtained with 15 Epstein-Barr virus positive lymphoblastoid cell lines, 4 T cell lines, a chronic myelogenous leukemia cell line, 4 teratoma cell lines, and one each of melanoma and neuroblastoma. The 38.13 monoclonal antibody may be useful for diagnosis and specific immunotherapy of Burkitt lymphomas. (8 Refs)

3. IMMUNOLOGICAL ANALYSIS OF A CHROMOSOMAL ANTIGEN SPECIFIC TO HUMAN GRANULOCYTES.

Ramage KC, Dunn JH, Campbell AM
Dept. Biochemistry, Univ. Glasgow, Glasgow G12 8QQ, Scotland
Biochem J; 203(1):235-238 1982

A chromosomal protein antigen specific for human granulocytes is described. The antigen is present in large amounts in granulocytes and in granulocytic leukemia. It is absent from HeLa cells, human fibrosarcoma cells and human lymphocytes. It is, however, present in small amounts in other human hemopoietic cell lines. The antigen binds tightly to DNA and requires the presence of DNA to react with the antibody. (Author abstract) (9 Refs)

4. ANALYSIS OF ANTIGENIC DETERMINANTS ON HUMAN MONOCYTES AND MACROPHAGES.

Todd RF, Schlossman SF
Div. Tumor Immunology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115
Blood; 59(4):775-786 1982

Mo1, 2, 3, and 4, and Plt-1 are a series of five distinct antigens detected on the surface of human peripheral blood monocytes by mouse monoclonal antibodies. Mo2 and 3 are restricted to the monocyte-macrophage series, while Mo1, as previously reported, is also expressed by human granulocytes and null cells. Mo3, as distinguished from Mo1 and Mo2, is weakly expressed by virgin peripheral blood monocytes but becomes well expressed if monocytes are cultured overnight at 37 C. Mo4 is coexpressed by monocytes and platelets, while Plt-1 appears to be a platelet-specific antigen whose detection on monocytes reflects adherence of platelets to monocyte membranes. That Mo2-4 are true monocyte antigens is demonstrated by their resynthesis following protease treatment of monocytes (Mol expression is resistant to proteolytic digestion). During myeloid-monocyte differentiation, the Mo antigens are infrequently expressed by immature myeloid cells but are found at higher frequency on leukemic monocytic forms. Macrophages from cultured peripheral blood monocytes and HL-60 cells exposed to lymphokines or phorbol diester express Mo1-4, but noncirculating peritoneal macrophages lack Mo3. the Mo antigens are differentiation markers whose expression reflects membrane heterogeneity during myeloid-monocyte-macrophage maturation. (Author abstract) (36 Refs)

5. A HUMAN T-CELL ANTIGEN DEFINED BY XENOANTISERUM TO SEZARY LEUKEMIC CELLS: IMMUNOCHEMICAL AND FUNCTIONAL STUDIES.

Ogasawara M, Ishii Y, Kamiya H, Kikuchi K
Dept. Pathology, Sapporo Medical Coll., S1 W17 Sapporo 060, Japan
Am J Hematol; 12(2):95-107 1982

Xenoantiserum to Sezary cell leukemia cells (ASS) was developed by immunizing rabbits with those cells and was absorbed with human red cells, liver, tonsil B cells, and cultured Raji cells. This reagent reacted by immunofluorescence with virtually all human thymus and T cells. In the thymus, medullary cells reacted more strongly with ASS than did cortical thymocytes. When immunoprecipitates that formed between ASS and 125I-labeled lymphocyte surface glycoproteins were analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, it was found that ASS precipitated a 72K mol wt (MW) glycoprotein from T cells but not from B cells. On the other hand, it was shown by functional studies that T cells sensitive to the cytotoxic effect of ASS contained T cells that could aid the immunoglobulin synthesis of B cells induced by pokeweed mitogen. On the other hand, suppressor T cells induced by concanavalin A resided in those cells rather resistant to its cytotoxic effect. These data support the idea that the 72K MW glycoprotein on human thymus and T cells might be homologous to mouse Lyt-1 antigens. (Author abstract) (27 Refs)

6. A DIFFERENTIATION ANTIGEN EXPRESSED SELECTIVELY BY A PROPORTION OF HUMAN BLOOD CELLS: DETECTION WITH A MONOCLONAL ANTIBODY.

Brooks DA, Bradley J, Zola H
(c/o Zola) Dept. Clinical Immunology, Flinders Medical Centre, Bedford Park 5042, Australia
Pathology; 14(1):5-11 1982

A monoclonal antibody, FMC 8, has been prepared after immunization with a cell line of the non-T-non-B type acute lymphoblastic leukemia (ALL). The antigen detected by this antibody consists of a single polypeptide chain with an apparent mol wt of 24,000 d. The antigen is absent from T cells but appears after mitogen stimulation. It is found on the majority of normal circulating B cells but is absent in most chronic lymphocytic leukemias. All cells of the non-T-non-B type express the antigen, whereas T-ALL cells generally do not. Granulocytes, monocytes and platelets react with the antibody, but erythrocytes do not. The wide but selective distribution of the antigen renders FMC 8 potentially useful, together with other monoclonal antibodies, in the delineation of differentiation pathways and in phenotypic analysis of leukemia and lymphoma cells. (Author abstract) (28 Refs)

7. A 94,000-DALTON GLYCOPROTEIN EXPRESSED BY HUMAN MELANOMA AND CARCINOMA CELLS.

Imai K, Wilson BS, Bigotti A, Natali PG, Ferrone S
(c/o Ferrone) Dept. Pathology and Surgery, Columbia Univ., 630 West 168th St., New York, NY, 10032
JNCI; 68(5):761-769 1982

The IgG2a monoclonal antibody (MoAb) 376.96S, secreted by a hybridoma derived from a mouse immunized with cultured human melanoma cells COLO 38, reacts with a single 94,000-dalton glycoprotein that is peripherally associated with the plasma cell membrane of cultured melanoma cells. Indirect immunofluorescence analysis with cryostat thin sections of human tissues showed that this antigen is absent from a large variety of normal tissues but is readily detectable on melanomas, nevi, and several different carcinomas. The MoAb376.96S binds with cultured melanoma and carcinoma cell lines to a similar extent and can mediate both complement-dependent and cell-dependent lysis of these cells. The 94,000-dalton glycoprotein detected by MoAb376.96S is distinct in its tissue distribution, antigenicity, and molecular profile from several structures previously identified with monoclonal antibodies that have similar molecular weights. (Author abstract) (24 Refs)

8. IDENTIFICATION AND PURIFICATION OF A MR 75,000 CELL SURFACE HUMAN MELANOMA-ASSOCIATED ANTIGEN.

Heaney-Kieras J, Bystryn JC
(c/o Bystryn) Dept. Dermatology, New York Univ. Sch. Medicine, New York, NY, 10016
Cancer Res; 42(6):2310-2316 1982

Surface macromolecules on cultured human melanoma cells were radioiodinated by a lactoperoxidase method. Macromolecules shed into culture medium were collected, concentrated, and fractionated on Sepharose 6B and lentil lectin-Sepharose. Radioactivity associated with macromolecules was assayed by precipitation with trichloroacetic acid, and that associated with melanoma-associated antigens (MAA) was assayed by specific immunoprecipitation with xenogeneic anti-melanoma serum. Following the last step in purification, approx two-thirds of the acid-soluble radioactivity in the most MAA-active fraction was associated with this antigen. MAA concentration in this fraction was approx 200-fold greater than that in cells, and it contained a single labeled protein band by polyacrylamide gel electrophoresis in sodium dodecyl sulfate. The MAA was a glycoprotein consisting of a single polypeptide chain with a mol wt of approx 75,000. This antigen was common to several but not to all melanomas. It was not detected, or was present in much decreased concentration, in 16 other unrelated allogeneic or xenogeneic normal and malignant cells. It was immunologically unrelated to serum albumin or fibronectin. These observations indicate that we have highly purified a Mr 75,000 cell surface component of human melanoma cells which appears to be a MAA. (Author abstract) (38 Refs)

9. GD3, A PROMINENT GANGLIOSIDE OF HUMAN MELANOMA. DETECTION AND CHARACTERIZATION BY MOUSE MONOCLONAL ANTIBODY.

Pukel CS, Lloyd KO, Travassos LR, Dippold WG, Oettgen HF, Old LJ
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
J Exp Med; 155(4):1133-1147 1982

Mouse monoclonal antibody AbR24 has a high degree of specificity for human melanoma cells when tested on viable cell cultures. The protein A mixed hemagglutinin serological assay demonstrated an antigen detected AbR24, shown to be GD3 ganglioside by compositional and partial structural analysis and by comparison with authentic GD3 in thin layer chromatography. AbR24 reacted with authentic GD3 but not with any of the other standard gangliosides tested. Melanomas have a characteristic pattern of gangliosides; in all lines examined, glycolipids comigrating with GD3 and GM3 were prominent acidic glycolipids, with GD3 being the major component in many of the lines. GD3 was also prominent in extracts of mouse eye and bovine choroid. The only other line that had GD3 as the major component was MOLT-4 (a T cell line). Compared with 7% in the adult human brain, 9% in a renal cancer cell line, 11% in RAJI cells, and 33% in MOLT-4 cells, GD3 constituted 18-63% of the total ganglioside fraction in the melanoma cell lines. The 125I-protein A mixed hemagglutinin serological assay detected GD3 in all the cells and tissues examined. The apparent discrepancy between the ubiquitous presence of GD3 and the serological specificity of AbR24 for melanoma cells was explained by the localization and concentrations of GD3 in different cells. (31 Refs)

10. TISSUE DISTRIBUTION AND MOLECULAR PROFILE OF A DIFFERENTIATION ANTIGEN DETECTED BY A MONOCLONAL ANTIBODY (345.134S) PRODUCED AGAINST HUMAN MELANOMA CELLS.

Imai K, Natali PG, Kay NE, Wilson BS, Ferrone S
(c/o Ferrone) Dept. Pathology, Coll. Physicians and Surgeons, Columbia Univ., 630 West 168th St., New York, NY, 10032
Cancer Immunol Immunother; 12(2):159-166 1982

The mouse IgG2a monoclonal antibody (MoAb) 345.134S secreted by a hybridoma derived from a mouse immunized with cultured human melanoma cells was examined in relation to the structure of the target antigen, the distribution of the antigen in normal and malignant tissues, and the expression of the antigen on cultured cells and its ability to function as a target of immune lysis. The structure detected by the MoAb 345.134S is composed of an 85 kilodalton (KD) glycopolypeptide linked by disulfide bridges with a 30 KD polypeptide carrying little or no carbohydrate. The 115 KD antigen appears to be peripheral rather than integral to the plasma membrane. Indirect immunofluorescence studies showed that the reactivity pattern of normal tissues with MoAb 345.134S does not correlate with their embryological origin. The majority of normal tissues gave only weak staining with MoAb 345.134S. All the types of tumors tested, except liver adenocarcinomas, reacted strongly with MoAb 345.134S, although there were some cases within each tumor group that were negative. MoAb 345.134S reacted in a radioimmunometric assay with a variety of cell lines, including melanoma, carcinoma, and lymphoid types. There was no relationship between the level of expression of the antigenic determinant recognized by MoAb 345.134S and other surface markers tested. The level of antigen detected by MoAb 345.134S was unchanged in the presence of interferon but was decreased by puromycin exposure. The opposite was true for cell-dependent lysis of cultured human cells. (32 Refs)

11. MOLECULAR HETEROGENEITY OF A HIGH MOLECULAR WEIGHT HUMAN MELANOMA ASSOCIATED ANTIGEN DETECTED BY MONOCLONAL ANTIBODIES.

Imai K, Wilson BS, Ruberto G, Nakanishi T, Yachi A, Ferrone S
Dept. Moleuclar Immunology, Scripps Clinic and Res. Foundation, La Jolla, CA
Protides Biol Fluid Proc Colloq; 29:893-897 1982

The spatial relationship among antigenic determinants recognized by four monoclonal antibodies (MoAbs) specific for a human high mol wt melanoma-associated antigen (MAA) was analyzed. The four MoAbs were compared in direct and indirect inhibition binding assays to determine whether they identified the same or different antigenic determinants. MoAbs 138.13S, 225.28S, and 653.40S recognized the same or closely associated antigenic determinants which were distinct from that recognized by MoAb 763.24T. Sequential immunodepletion studies demonstrated that the high mol wt MAA may be divided into three subpopulations: Group 1 carries the antigenic determinants recognized by the MoAb 138.13S (225.28S or 653.40S) and 763.24T; Group 2 carries only the determinants recognized by MoAb 138.13S (225.28S or 653.40S); and Group 3 carries only the determinants recognized by the MoAb 763.24T. The amount of high mol wt molecules in each subpopulation was in the order of Group 1 greater than Group 2 greater than Group 3. (7 Refs)

12. FIVE MELANOMA-ASSOCIATED ANTIGENS IDENTIFIED BY MONOCLONAL ANTIBODIES.

Hellstrom KE, Hellstrom I, Brown JP, Yeh MY, Woodbury RG
Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
Protides Biol Fluid Proc Colloq; 29:877-882 1982

Mice were immunized with human melanomas and hybridomas were established that identify cell surface antigens. Five antigens were identified by monoclonal antibodies: antigens 3.1, p97, p155, p210, and 4.2. These antigens are described with respect to antibody, molecular nature, and specificity in cultured cells and biopsies. Antigen 3.1 is thought to be a glycolipid and exhibits specificity for a small subgroup of cultured melanomas and biopsy material from melanomas and normal tissues. Antigen p97 is a 97,000 mol wt glycoprotein with specificity for approx 50% of cultured melanomas and biopsy tissue from approx 50% of biopsied melanomas and some fetal tissues. Antigen p155 is a 155,000 mol wt protein (possibly a glycoprotein) and exhibits specificity in cultured and biopsied melanomas. Antigen p210 is a 210,000 mol wt protein (possibly a glycoprotein) exhibiting specificity in approx 30% of cultured melanomas and 25% cultures of other tumors and in biopsies of melanomas, other tumors, and adult and fetal brain. Antigen 4.2 may be a glycolipid and exhibits specificity for approx 80% of cultured melanomas and a few other tumors. The implications of these findings in diagnosis and therapy of human melanomas and other tumors are discussed. (24 Refs)

13. STUDIES ON ANTIGENS IN CANCER OF HUMAN BUCCAL MUCOSA.

Chatterjee R, Guha S, Bose SR
Dept. Tumor Immunobiology, Chittaranjan Natl. Cancer Res. Centre, Calcutta 700 026, India
Indian J Exp Biol; 19(12):1107-1109 1981

Antisera were raised in rabbits against an antigenic extract (Ca Ag) prepared from pooled cancerous tissue from the buccal mucosa of 8 patients with carcinoma of the lip, tongue, and maxilla. Prior to absorption with various agents, antisera showed multiple precipitin lines; after absorption, only one band with Ca Ag was observed and no bands were seen with the other antigens studied. The antigen is presumed to be tumor-specific (associated) for buccal mucosa. Immunoreactivity of Ca Ag was not altered by exposure to 60 C for 30 min or by pH stress at 5.52 and 9.19. (15 Refs)

14. PATTERNS FOR NORMAL COLON MUCOSA AND COLON ADENOCARCINOMA COMPARED BY TWO-DIMENSIONAL GEL ELECTROPHORESIS.

Tracy RP, Wold LE, Currie RM, Young DS
Section Clinical Chemistry, Mayo Clinic, Rochester, MN, 55905
Clin Chem; 28(4,part2):915-919 1982

A two-dimensional gel 'map' of the proteins in normal cells and transformed cells may well help establish the presence of putative tumor-specific protein antigens, which can be isolated and used as antigens. We so examined normal colon mucosa and colon adenocarcinoma, using a sensitive silver stain. Samples were promptly prepared after excision by rapidly trimming the tissue to a small, grossly homogeneous piece, which was frozen on solid CO2. Frozen histological sections and permanent mounts were also prepared for several areas, to document the cellular constitution and to grade the carcinoma. Sample preparation for electrophoresis is described. The DNA was pelleted by centrifugation (108,000 X g X 1.5 hr). Little or no pellet was observed, indicating complete solubilization. Many of the tumors contained proteases, liberated during sample preparation, so protease inhibitors were included. A highly reproducible pattern was observed for normal mucosa. Comparison of the gels from paired samples with histological data allows many of the spots to be tentatively assigned to the different cell types present in the mucosa (epithelium, connective tissue, or muscularis mucosa) and, in most tumors analyzed, detection of a series of spots that are not detectable in the pattern for normal tissue. These apparently tumor-associated proteins may be of epithelial cell or stromal origin. (Author abstract) (13 Refs)

15. PREPARATION AND CHARACTERIZATION OF MONOCLONAL ANTIBODIES AGAINST ANTIGENS OF HUMAN RENAL ADENOCARCINOMA.

Hess H, Alheid U, Biermann S, Waks T, Scherberich JE, Mondorf AW, Schoeppe W, Senge T, Falkenberg FW
Dept. Nephrology, Center for Internal Medicine, Klinikum J. W. Goethe Universitat, 6000 Frankfurt am Main, W. Germany
Protides Biol Fluid Proc Colloq; 29:903-905 1982

Lymphocytes from BALB/c mice hyperimmunized by four and eight consecutive injections of renal adenocarcinoma plasma membranes were fused with X63-Ag 8.653 plasmacytoma cells. In the supernatants of 90/600 wells with viable cells, antibodies reactive with antigens in tumor and/or kidney were found. Twenty-two clones were isolated and characterized. Tumor cell membranes, capillaries and intercellular matrix were recognized by the various monoclonal antibodies. Generally, the density of antigenic determinants was higher in the tumor than in normal kidney tissue. No monoclonal antibodies were found that reacted exclusively with tumor. Localization of antigenic determinants in the kidney was easy, while in the tumor tissue localization could not be defined exactly. Antibodies of Hyp I 164 D5 and Hyp I 289 A1 reacted with tumor cell membranes, antibody Hyp I 238 A9 with capillaries. (5 Refs)

16. INFLUENCE OF THE LIVER ON THE PROFILE OF CIRCULATING ANTIGENS RECOGNIZED BY ANTISERUM AGAINST HEPATOMA MEMBRANE GLYCOPROTEINS.

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Dept. Cell and Tumor Biology, Roswell Park Memorial Inst., Buffalo, NY, 14263
Cancer Res; 42(6):2398-2406 1982

Rat hepatoma tissue culture cells have retained only a few liver-specific membrane functions. To find out whether transformation of these cells led to the appearance of tumor-specific membrane glycoprotein structures, which might also be present in released form in the circulation of tumor-bearing animals, we compared immunologically the sera and ascites fluids of normal and of hepatoma-bearing rats. For structural identification, we used polyspecific antibodies against the membrane glycoproteins of the hepatoma cells. Crossed immunoelectrophoresis of the body fluids resulted in the separation of several antigens, one of which appears to be tumor specific. Immunoelectrophorectic analyses of the glycoproteins from the membranes of liver and hepatoma cells revealed many shared antigens; in one instance, we could assign the membrane associated form to major antigen detected in the serum. Characterization of the molecular size and charge of two selected antigens by two-dimensional gel electrophoresis indicated that the hepatoma cell products were not completely sialylated. In the case of the circulating, hepatoma-specific antigen, this property appears to result in hepatic clearance of the most basic ('asialo') portion of the glycoprotein species via the receptor-mediated uptake of galactose-terminated glycoproteins. The result was the accumulation of the acidic forms of the antigen in the serum and ascites fluid of tumor-bearing rats. (Author abstract) (19 Refs)

17. IMMUNOLOGIC RECOGNITION OF CELL SURFACE ANTIGENS IN NORMAL MOUSE NEURAL TISSUES AND IN NEUROEPITHELIAL CELLS OF THE OTT-6050 MOUSE TERATOMA. A RADIOMETRIC, GEL ELECTROPHORETIC, AND MORPHOLOGIC (IMMUNOFLUORESCENCE AND IMMUNOPEROXIDASE) STUDY.

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Acta Neuropathol (Berl); 56(3):214-224 1982

Use of the immunoperoxidase method for recognition of neural cell surface antigens (SA) was studied. Membrane fractions were prepared from neural tissues, liver, spleen, kidney, heart, testes, and thymus of adult and neonatal F1(129/J x C3H/HeJ) mice and from three OTT-6050 mouse teratoma-derived tumors. Antiserum to neural SA was produced in New Zealand white rabbits by injection of membrane preparations. The antiserum cross-reacted with SA of neuroblasts and primitive and mature glial cells, as indicated by radioimmunoassays. Binding of the antiserum to neonatal brain membranes was almost completely eliminated by preabsorption on adult mouse brain membranes; binding was not reduced by preabsorption on liver, spleen, kidney or heart membranes. Antiserum cross-reacted with certain non-neural tissue types including sperm and sperm-precursor cells, some epithelial cells in the medulla of adult mouse thymus, and various mesenchymal cells in neonatal mice. Binding of antiserum to brain membranes was slightly reduced by preabsorption with testis pellets or thymus cells. Cross-reactivity was eliminated by preabsorption with adult brain membranes. Preabsorption with testis pellets or thymus cells reduced staining of primitive neuroepithelial cells in teratoma-derived tumors; staining of neural cells in the mature neuropil was reduced but not eliminated. Polyacrylamide gel electrophoresis identified major protein bands at mol wt 26,000, 32,000, 40,000, 42,000, 45,000, and 54,000 daltons. Results of autoradiographic analysis indicated that the antiserum reacted only with minor protein components of mouse brain membranes. (38 Refs)

18. REGULATION OF THE CELLULAR P53 TUMOR ANTIGEN IN TERATOCARCINOMA CELLS AND THEIR DIFFERENTIATED PROGENY.

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Mol Cell Biol; 2(4):443-449 1982

The regulation of a 53,000-mol wt cellular tumor antigen, p53, in F9 embryonal carcinoma cells was investigated. Treatment of F9 cells with retinoic acid and dibutyryl ADP causes the cells to differentiate, predominantly into endoderm-like cells, and results in a marked decrease in the levels of p53. The mechanism(s) responsible for the decline in p53 in differentiated cells involves a marked decrease in the amount of in vitro translatable p53 messenger RNA. This mechanism is discussed with respect to that operating in simian virus 40 infection or transformation and which involves increased stability of the p53 protein. (22 Refs)

19. NEW CARBOHYDRATE ANTIGEN FOUND IN LARGE GLYCOPEPTIDES OF TERATOCARCINOMA CELLS.

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Biochem Biophys Res Commun; 105(2):495-501 1982

A cell surface carbohydrate antigen from murine teratocarcinoma OTT6050 was investigated and compared to surface antigens from other cancer cells and adult tissues. Glycoproteins were isolated by affinity chromatography on agarose-conjugated Dolichos biflorus agglutinin (DBA), a lectin specific for the alpha-N-acetylgalactosaminyl residue. From rabbit antiserum against DBA receptors of OTT6050, specific antibodies reacting with the large glycopeptide from F9 embryonal carcinoma cells were isolated by immuno-affinity chromatography on a column containing the Sepharose-immobilized OTT6050 glycopeptide. The antigen(s), whose antigenic determinant was assumed to be N-acetylgalactosamine based on its DBA binding activity, was designated as TC (teratocarcinoma-derived carbohydrate) antigen. Molecules carrying TC antigen from OTT6050 and from F9 migrated as glycoproteins of apparent mol wt more than 300,000 upon sodium dodecyl sulfate gel electrophoresis. Immunofluorescence using the purified anti-TC antibodies detected the TC antigen in the stem and endothelial cells of OTT6050, GRSL leukemia cells, and 2-4 cell mouse embryos. The antigen was not detected in morulae or any of several adult tissues tested. TC antigen can be distinguished from other antigens found in embryo carcinoma cells, eg SSEA-1 and F9. Its absence from sheep and human erythrocytes also distinguishes the TC antigen from Forssman, ABH, and I antigens. TC antigen should prove to be a useful marker in embryological and oncological studies. (21 Refs)

IMMUNOLOGICAL STUDIES

20. HUMAN-MOUSE HYBRIDOMA CELLS PRODUCING ANTIBODIES.

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Protides Biol Fluid Proc Colloq; 29:609-614 1982

Xenogeneic hybridomas between human lymphocytes and mouse myeloma cells were produced and the effects of various factors on their growth were studied. After fusion, cells were resuspended in culture medium containing 10% human endothelial culture supernatant (HECS) and when hybrid clones developed, the supernatants were tested for the presence of antibodies against RhD+ RBC. The hybridoma cells producing anti-D activity were expanded and cloned by limiting dilution in culture medium containing 10% HECS. Six days of culture in the presence of pokeweed mitogen strongly increased the yield of hybridoma cells. The recovery of hybridoma cells producing anti-D antibodies was significantly increased by culturing the lymphocytes in the presence of RhD+ RBC together with endothelial cells. All eight hybridoma supernatants agglutinating RhD+ RBC had specificity for the D antigen. Specific antibody production decreased markedly with time, indicating the instability of the xenogeneic hybridoma cells. Selection for antibody-producing clones was accomplished by culturing at low density and discarding negative clones. The percentage of wells containing hybridoma cells producing anti-D antibodies increased upon each passage up to the fourth passage, when a plateau was reached. Thus, when lymphocytes obtained from persons who had been immunized with allogeneic RhD+ RBC were fused with mouse myeloma cells, hybridoma cells were obtained producing specific anti-D antibodies. (13 Refs)

21. DIFFERENTIATION OF HUMAN T LYMPHOCYTES: II. PHENOTYPIC DIFFERENCE IN SKIN AND BLOOD MALIGNANT T-CELLS IN CUTANEOUS T-CELL LYMPHOMA.

Haynes BF, Hensley LL, Jegasothy BV

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J Invest Dermatol; 78(4):323-326 1982

The cell surface antigen phenotype of circulating and skin malignant T-cells in patients with cutaneous T-cell lymphoma were studied. The mature T-cell antigen phenotype of the malignant T-cells was identical for circulating and skin malignant T-cells. In contrast, skin malignant T-cells expressed the immature human T-cell antigen Thy-1, surface membrane transferrin receptors, and Ia-like determinants while circulating malignant T-cells did not express these antigens. Skin infiltrating T-cells in benign dermatoses also expressed Thy-1 and Ia-like determinants. These observations support the notion that the skin is a major site of extrathymic T-cell differentiation and may promote phenotypic changes in circulating T-cells that home to skin. (Author abstract) (24 Refs)

22. DEGRADATION OF TUMOR-ASSOCIATED ANTIGENS SHED BY HUMAN MELANOMA CELLS IN CULTURE.

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Cancer Res; 42(6):2121-2125 1982

The fate of cell surface tumor-associated antigens shed by viable human melanoma cells was studied in vitro. Labeled surface material shed by radio-iodinated melanoma cells was incubated with a variety of unlabeled human cells for 24 hr. Both melanoma-associated antigens (MAAs), quantitated by specific immunoprecipitation, and unrelated surface macromolecules were degraded or inactivated by normal and malignant cells including the melanoma cells themselves. The MAAs studied were particularly susceptible to degradation. Following incubation with a variety of cells, immunoreactive MAAs decreased 2 to 3 times more rapidly than did unrelated surface macromolecules shed concurrently by melanoma cells. However, melanoma cells had a selective defect in their ability to degrade MAAs. Though catabolically active, these cells degraded non-MAA surface macromolecules shed by themselves or by allogeneic cells much more rapidly than they activated MAAs. These observations suggest that the ultimate amount of soluble tumor antigens that accumulate in body fluids will depend on the balance between the rate of their release and that of their degradation and that as a result of a selective defect in the catabolic activity of melanoma cells some tumor antigens may be particularly prone to accumulate in the extracellular fluid bathing these tumors. (Author abstract) (33 Refs)

23. MONKEY (MACACA SPECIOSA) ANTISERA AGAINST MELANOMA. FAILURE TO DEMONSTRATE SPECIFIC ANTIBODIES AGAINST COMMON MELANOMA-ASSOCIATED MEMBRANE ANTIGENS.

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Cancer Immunol Immunother; 12(2):153-158 1982

The specificities of eight monkey antisera prepared with cultured melanomas and soluble membrane extracts of melanoma tissue were examined. With partially absorbed monkey antisera, there were positive reactions with many melanomas and negative reactions with control adult, embryonal, and non-melanoma cells. However, antibodies against normal lymphocytes could still be detected. After continued absorption with buffy coat cells, positive reactions were found with only a few of the melanoma cell lines. In the indirect membrane immunofluorescence test, the absorbed antisera reacted with melanoma and control cells. Melanoma-associated antigens were not found after absorption with cultured control tumor cells, fetal calf serum, and liver. The F(ab')2 fragments were directed against IgG immunoglobulins. The results gave no evidence of the presence of specific antibodies against common melanoma-associated antigens in the antisera derived from hyperimmunized monkeys. (30 Refs)

24. CLINICAL ASPECTS OF GASTROINTESTINAL MUCUS.

Forstner G, Wesley A, Forstner J
Kinsmen Cystic Fibrosis Res. Centre, Hosp. for Sick Children, Toronto, Canada
Adv Exp Med Biol; 144:199-224 1982

Histochemical studies of gastrointestinal mucus in peptic ulcer disease, parasitic infections, cystic fibrosis, adenocarcinoma, and inflammatory bowel disease are reviewed. Evidence, particularly in the colon, suggests that mucins produced by adenocarcinoma and even transitional mucosa in the neighborhood of the tumor are abnormal. Sialomucins are increased at the expense of sulfomucins. Mucins produced by tumor cells share antigenic determinants with mucus glycoproteins from normal tissue. Antisera to the colonic mucoprotein precipitate antigens from adenocarcinoma extracts. (110 Refs)

25. HETEROZYGOSITY AT GM LOCI ASSOCIATED WITH HUMORAL IMMUNITY TO OSTEOSARCOMA.

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J Exp Med; 155(4):1228-1232 1982

The possible role of Gm allotypes (genetic markers of IgG) in predisposition to osteosarcoma was investigated. Blood was collected from 50 patients with osteoblastic sarcomas and the presence of osteosarcoma-associated antigens (OSAA) was studied and Gm allotyping was performed. Of the five Gm phenotypes present in the blood, none were significantly associated with osteosarcoma. Two Gm phenotypes (Gm 3;5,13,14 and Gm 1,3,17;5,13,14,21) were significantly associated with immune response to OSAA: the first was associated with no detectable antibody (8% positive and 63% negative) and the second was clearly associated with detectable antibodies to OSAA (83% positive and 11% negative). Since the most probable genotype of the Gm 3;5,13,14 phenotype is Gm 3;5,13,14/Gm 3;5,13,14 and that of Gm 1,3,17;5,13,14,21 is Gm 1,17;21/Gm 3;5,13,14, it was postulated that two Ir genes were in linkage disequilibrium with the Gm 1,17;21 and Gm 3;5,13,14 haplotypes. Possession of either gene alone would not confer humoral responsiveness to OSAA; however, in the heterozygous condition (Gm 1,17;21/Gm 3;5,13,14) the genes would complement to permit a humoral response to OSAA. (23 Refs)

26. THE INFLUENCE OF ANTIGEN DENSITY AND A COMPARISON OF IGG AND IGM ANTIBODIES IN THE ANTI-COMPLEMENTARY MODULATION OF LYMPHOCYTIC SURFACE IMMUNOGLOBULIN.

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Scand J Immunol; 15(2):169-177 1982

Experiments were carried out to determine the influence of antigen density on anti-complementary modulation, defined here as the conferring by anti-immunoglobulin (Ig) of resistance to lysis of guinea pig L2C leukemic lymphocytes through anti-Ig plus syngeneic complement (C). Populations of leukemic cells varied widely in their quantitative expression of surface membrane Ig as judged by the binding to cells of 125I-labeled Fab' fragments from anti-Ig, and a good correlation between the bulk antigen density and the percentage of cells lysed by anti-Ig plus C was obtained ($p = 0.02$). In the presence of 10 mM sodium azide, which has been shown to diminish the modulation occuring during simultaneous incubations with anti-Ig and C, this correlation was even stronger (p less than 0.001). No zone could be defined in which the level of surface Ig expression was sufficient to serve complement lysis but too low for modulation. Furthermore, both the degrees and rates of modulation occurring on incubation with antibody at 37 C, either before C addition or in the presence of lytic C, were similar for populations of high, low, or intermediate antigen density. Separation of cells by their size or density failed to yield populations differing in either their susceptibility to humoral killing through anti-Ig or their modulating capacity. IgG and IgM antibodies to the L2C cell surface Ig evoked similar levels of killing with syngeneic C, and when compared for their ability to promote anti-complementary modulation, no difference was revealed in either the rate or degree of modulation occurring during incubations at 37 C with the two isotypes. The findings are discussed with particular reference to observations on the modulation of mouse thymus leukemia (TL) antigens. (Author abstract) (38 Refs)

27. CHARACTERIZATION OF SOME ANTIGENS ASSOCIATED WITH THE MEMBRANE OF HAMSTER TUMOR CELLS.

Duthu A, Alexandrov I, Haddada H, Le Goffic N, Zuinghedau J, De Vaux Saint Cyr C
Institut de Recherches Scientifiques sur le Cancer (B.P. n), 8-94800 Villejuif, France
Protides Biol Fluid Proc Colloq; 29:159-162 1982

An in vitro antigen dosage was determined which characterized antigens present at the surface of nine syngeneic and nonsyngeneic lines of hamster tumor cells. The results were correlated with the findings observed with the in vivo action of immunized lymphocytes in the Winn neutralization test. The cells were tested against a panel of antisera obtained from tumor-bearing hamsters or from hamsters immunized against the different cell lines maintained in cell culture. Antibody fixation on the surface of the living cells was determined by the amount of 125I-labeled staphylococcal protein A fixed on the cells. With use of the modified Winn test, splenic lymphocytes from immunized or normal hamsters together with tumor cells were injected sc in a 100:1 ratio of lymphocytes:tumor cells into naive recipients. The specific antibody fixation was demonstrated by the difference in slopes of the fixation curves between antisera and controls. Results showed that besides virus-induced antigens, the Forssman-like antigen appeared to be the most common. In the Winn neutralization test, a strong protection was observed when homologous immune lymphocytes were used while a weak cross reaction was observed with other cells. Only a small percentage of animals were protected against the graft of heterologous cells, indicating the presence at the cell membrane of cross-reacting determinants able to elicit a weak tumor rejection. (12 Refs)

28. CYTOTOXICITY OF TUMOUR-BEARER SERUM TO D23 HEPATOMA CELLS DERIVED FROM SOLID TUMOURS, ASCITES OR IN VITRO CULTURES.

Lando P, Gabriel J, Berzins K, Perlmann P
Dept. Immunology, Univ. Stockholm, Stockholm, Sweden
Scand J Immunol; 15(3):259-266 1982

The complement-dependent cytotoxicity of antibodies in tumor-bearer serum (TBS) from rats carrying the chemically induced D23 hepatoma was investigated. Target cells were D23 cells from solid tumors (D23sol), from ascites tumors (D23asc), or from in vitro growing cell cultures (D23cc). The D23asc and D23cc cells were not lysed when used as target cells in the assay, although they evoke cytotoxic antibodies when growing in vivo. The D23 ascites cells became susceptible to complement-dependent lysis after trypsin treatment. This was, however, not due to unmasking of target antigens, since untreated D23 ascites cells absorbed cytotoxic antibodies as efficiently as trypsinized cells. No increase in susceptibility to complement-dependent lysis was observed after trypsin treatment of D23cc cells. Absorption of cytotoxic antibodies with D23cc cells showed no or very low antigen expression on the surface of these cells. They did, however, contain the antigen(s), since 3 M KCl extracts of the D23cc cells could inhibit the complement-dependent cytotoxicity of D23sol TBS against D23sol cells. From these data it was concluded that the susceptibility of hepatoma cells for antibody-mediated complement lysis is not only correlated with antigen expression, as was the case with the in-vitro-cultivated cells, but is also dependent on increased lytic susceptibility after trypsin treatment of the cells. (Author abstract) (26 Refs)

29. REVERSAL BY CITROVORUM FACTOR OF METHOTREXATE-INDUCED SUPPRESSION OF CELL-MEDIATED AND HUMORAL IMMUNE RESPONSE IN MOUSE MODEL SYSTEMS.

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Biochem Pharmacol; 31(7):1387-1392 1982

C3H/HeHa mice were immunized (day 0) with 5 x 10(8) sheep red blood cells (SRBC) or 3 x 10(7) EL-4 lymphoma cells (ip), and C57Bl/6J mice were immunized (day 0) with 3 x 10(7) P815 mastocytoma cells (ip). Methotrexate (MTX, 100 mg/kg) was given ip on day +2, with or without citrovorum factor (CF) at equimolar dose. In the absence of CF in C57Bl/6J mice, the complement-independent cellular cytotoxicity (CICC) response did not recover in 18 days from MTX suppression to levels seen in immunized controls, while in C3H mice, with EL-4 as antigen, the response equalled that of controls by day 18 and was similar to or greater than that of controls through day 28; in both cases the serum antibody response returned to control levels by day 20. In both mouse strains, CF produced immediate recovery of the responses measured. In contrast, with SRBC as antigen, while the MTX suppression of complement-dependent cellular cytotoxicity (CDCC) in the absence of CF recovered by day 7, the CICC response recovered much more slowly. CF administration produced a rapid (day 4) return of CDCC activity to control levels, but only a partial restoration of CICC activity by day 6. In conclusion, the kinetics of recovery of the CICC and CDCC responses and of CF rescue of MTX-induced immunosuppression were dependent on mouse strain and on immunogens used, as well as on the type of response measured. Thus, selectivity of MTX action is indicated. (Author abstract) (25 Refs)

VIRUS ASSOCIATED ANTIGENS

30. MONOCLONAL ANTIBODIES TO EPSTEIN-BARR VIRUS-INDUCED, TRANSFORMATION-ASSOCIATED CELL SURFACE ANTIGENS: BINDING PATTERNS AND EFFECT UPON VIRUS-SPECIFIC T-CELL CYTOTOXICITY.

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Int J Cancer; 29(4):373-381 1982

Spleen cells from mice immunized with Epstein-Barr virus-transformed lymphoblastoid cells (EB-LCL) were used to generate monoclonal antibodies to cell surface antigens associated with the EB virus-transformed state. Radioimmune and immunofluorescence binding assays identified two antibodies, MHM6 and AC2, which reacted consistently with all EB-LCL tested, with a subpopulation of cells in some but not all EB virus genome-positive Burkitt lymphoma lines, but with none of a range of EB virus genome-negative cell lines of lymphoma or leukemia origin. While MHM6 appeared to bind an EB virus-related antigen, AC2 bound some other cell surface antigen which was also found on a small subpopulation of cells in lymphocyte cultures stimulated with phytohemagglutinin or with pokeweed mitogen. MHM6 and AC2 recognized single polypeptides with apparent mol wt of 45 kd and 80 kd respectively as shown by sodium dodecylsulphate polyacrylamide gel electrophoresis (SDS-PAGE) analysis of 125I-labeled cell surface polypeptides immunoprecipitated with these antibodies. These polypeptides were induced on experimentally-infected B cells within 24 hr of the expression of the EB virus nuclear antigen, EBNA, at a time known to coincide with the appearance of the lymphocyte-detected membrane antigen, LYDMA. However, saturating concentrations of MHM6 and of AC2 were unable to protect EB-LCL target cells from lysis by LYDMA-specific cytotoxic T cells in a chromium-release assay. (Author abstract) (50 Refs)

31. MIGRATION INHIBITION CAUSED BY EBV-SPECIFIC 48K SUBCOMPONENT OF EBNA AND THE ASSOCIATED 53K CELLULAR PROTEIN.

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Int J Cancer; 29(4):413-416 1982

Leukocytes from EBV-seropositive but not seronegative healthy donors responded with significant migration inhibition to the 48K subcomponent of the Epstein-Barr virus determined nuclear antigen (EBNA), known to carry the virally determined antigenic specificity. A concentration of 10 ug/ml was still effective while 5 ug/ml had no detectable effect. EBNA-associated cellular 53K protein had no effect by itself, but it potentiated the effect of 48K, even if the latter was added at the subliminal concentration of 5 ug/ml. The related 53K protein, isolated from EBV-negative human lymphoma cells, was also effective, whereas the corresponding murine-tumor-associated 53K had no potentiating effect. Immunization of mice with an extract of DNA-binding proteins from EBV-carrying Raji cells, known to contain both 48K and 53K, induced a significant macrophage migration inhibition response, to both human 48K and 53K. Murine 53K was ineffective, however. Human but not murine 53K increased the migration inhibitory activity of subliminal concentrations of 48K in the murine macrophage system as well. These findings suggest that human but not murine 53K may reconstitute with 48K (EBNA) to form a highly immunogenic complex. (Author abstract) (24 Refs)

32. MONOCLONAL ANTIBODY AGAINST EBV-ASSOCIATED TRANSFORMATION ANTIGEN DETECTED IN VITRO AND IN VIVO.

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Protides Biol Fluid Proc Colloq; 29:739-742 1982

Transformation antigens on the surface of in vitro Epstein-Barr virus (EBV)-transformed B lymphocytes were defined by producing specific monoclonal antibodies. A hybridoma (17D6) was cloned and analyzed for its binding properties to a variety of EBV-positive and -negative B cell lines. The antibody reacted strongly with all of the EBV-positive lines and weakly with the EBV-negative lines. Similarly, a panel of EBV-negative cell lines from a variety of sources reacted only weakly with the 17D6 antibody. When a whole panel of EBV-infected cells from sources other than in vitro infection were tested, all the cell lines containing EBV were as positive as in vitro infected cells, including one cell line derived by spontaneous outgrowth from an EBV-positive individual and one from co-cultivation of normal lymphocytes from a seronegative individual with a nasopharyngeal carcinoma. Burkitt's lymphoma tumor cells reacted only weakly with the 17D6 antibody due to their relatively low levels of the antigen. 17D6-positive cells also were detected in the peripheral blood of infectious mononucleosis (IM) patients. 17D6-positive cells could be detected in the peripheral blood of a patient with chronic EBV infection at higher levels than in patients with acute IM. After recovery, no 17D6-positive cells could be detected. Radioimmunoprecipitation studies suggested that the 17D6 antibody recognizes a polypeptide of 40,000 mol wt. The results indicated that the 17D6 antibody recognizes an EBV-associated transformation antigen on the surface of in vitro and in vivo infected cells. (4 Refs)

33. DISSECTION OF THE ANTIGENIC DETERMINANTS EXPRESSED ON THE CELL SURFACE OF RSV-TRANSFORMED FIBROBLASTS BY MONOCLONAL ANTIBODIES.

Ferracini R, Prat M, Comoglio PM
Univ. Trieste, Sch. Medicine, Trieste, Italy
Int J Cancer; 29(4):477-481 1982

Fusion of P3/X63-Ag8 mouse myeloma cells with splenocytes obtained from mice hyperimmunized with a BHK hamster fibroblast line transformed by an env-strain of Rous sarcoma virus (RSV) resulted in the production of antibody-secreting hybridomas. Seven hybrid clones secreted antibodies binding to RSV-transformed BHK fibroblasts but not to the parental control non-transformed line. The antibodies produced by three of these clones did identify antigenic determinants expressed also on BHK cells transformed by SV40. The antibodies produced by four other clones reacted specifically with cells transformed by RSV but not with cells productively infected by the transformation-defective Rous-associated virus-I; one of these reacted with RSV-transformed hamster cells only, three others identified antigenic determinants common to RSV-transformed cells of different animal species. These data give further support to the idea that RSV-transformed cells express a cell-surface antigen, specific for transformation, the expression of which is controlled by the transforming src gene, and that the specificities carried on it follow a complex pattern, arising from the interaction between antigenic determinants of cellular and viral origin. (Author abstract) (49 Refs)

34. P65 OF GAZDAR MURINE SARCOMA VIRUSES CONTAINS ANTIGENIC DETERMINANTS FROM ALL FOUR OF THE MURINE LEUKEMIA VIRUS (MULV) GAG POLYPEPTIDES (P15, P12, P30, AND P10) AND CAN BE CLEAVED IN VITRO BY THE MULV PROTEOLYTIC ACTIVITY.

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Virology; 118(2):380-388 1982

Thin-section electron micrographs of Gazdar murine sarcoma virus (Gz-MSV) particles showed that 100% of the particles possessed an immature morphology. Correspondingly, p65 (the major 65,000-dalton protein observed on sodium dodecyl sulfate-polyacrylamide gel electrophoresis for Gz-MSV particles) possessed antigenic determinants from all four of the murine leukemia virus (MuLV) Pr65gag polypeptides - that is, p30, p15, p12, and p10. This result is in contrast to earlier observations which reported that p65 lacked antigenic determinants of MuLV p10. It is consistent with the recent finding of Maxwell and Arlinghaus (1981) that Gz-MSV p65, when cleaved in vitro gives rise to a polypeptide with the size and antigenic determinant of MuLV p10. Thus, we suggest that Gz-MSV p65 should be designated as Gz-MSV Pr65gag. We also found that Gz-MSV Pr65gag could be cleaved in vitro by using a partially purified proteolytic factor that had been derived from Moloney murine leukemia virus (M-MuLV) by Sephadex G-75 column chromatography. Protein bands were produced that migrated on gels and had the same antigenic determinants as the MuLV intermediates Pr40gag (p30, p10) and Pr27gag (p15, p12). Pr55gag (p15, p12, p30), a minor component, was also produced. Additional incubation of Gz-MSV Pr65gag led to a breakdown of the intermediate polyproteins into the four MuLV gag polypeptides p30, p10, p15, and p12. The final processing of Pr55gag and Pr40gag occurred more rapidly than that of Pr27gag. It thus seems that in vitro sequentially different processing events are involved in production of the four internal gag antigens from Gz-MSV Pr65gag. (Author abstract) (23 Refs)

35. GENERATION OF CYTOTOXIC LYMPHOCYTES BY SV40-INDUCED ANTIGENS.

Chang C, Chang R, Mora PT, Hu C
Dept. Medical Res., Veterans General Hosp., Taipei, Taiwan, Republic of China
J Immunol; 128(5):2160-2163 1982

In order to study the correlation of in vivo tumor transplantation immunity and in vitro immunologic assays, cell-mediated cytotoxicity against SV40-transformed cells was studied in AL/N strain mice by using 51Cr-release assay. Killing of SV40-transformed AL/N fibroblast cells was observed by spleen cells of AL/N mice immunized with syngeneic SV40-transformed cells. Immunization with the solubilized SV40 tumor-specific transplantation antigen (TSTA) that induced transplantation immunity in vivo did not elicit cytotoxic spleen cells in vitro. However, the spleen cells from mice immunized with solubilized TSTA and then sensitized in vitro with SV40-transformed cells became cytotoxic against SV40-transformed fibroblasts. Similarly, SV40 TSTA (T antigen) purified by immunoprecipitation was able to prime the lymphocytes in AL/N mice: the primed lymphocytes could differentiate into cytotoxic lymphocytes upon in vitro stimulation by SV40-transformed cells. These data indicate that SV40 TSTA (T antigen) plays a role in the induction of cytotoxic lymphocytes. (Author abstract) (30 Refs)

36. INTRACELLULAR TRANSPORT OF SV40 LARGE TUMOR ANTIGEN: A MUTATION WHICH ABOLISHES MIGRATION TO THE NUCLEUS DOES NOT PREVENT ASSOCIATION WITH THE CELL SURFACE.

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Virology; 119(1):169-184 1982

The cT mutation of PARA, an SV40-adenovirus 7 hybrid virus, abolishes the transport of SV40 T-antigen (T-ag) to the nucleus and results in the accumulation of T-ag in the cytoplasm of infected and transformed cells. The effect of the cT mutation on the association of T-ag with the cell surface was examined in PARA(cT)-infected monkey cells. Surface-associated T-ag was detected by immunofluorescence, lactoperoxidase-catalyzed cell-surface iodination, and cellular fractionation. Surface-associated T-ag was more readily labeled by cell-surface iodination with PARA(cT)-infected cells than with SV40 and wild-type PARA [PARA(nT)]-infected cells. Control experiments eliminated the possibility that the enhanced detection of T-ag in PARA(cT)-infected cells was due to the labeling of intracellular T-ag by lactoperoxidase or to T-ag leaking from dead cells and adhering to the cell surface. The elevated level of surface-associated T-ag in PARA(cT)-infected cells was confirmed by metabolic labeling and cellular fractionation, indicating that the increased iodination of surface-associated T-ag was due to a greater number of T-ag polypeptides on the surface rather than a greater exposure of tyrosine residues. Pulse-chase experiments demonstrated that the elevated level of surface-associated T-ag in PARA(cT)-infected cells was not due to a prolonged stability of surface-associated T-ag. The cT mutation provides a useful tool for studies of mechanisms governing intracellular protein transport. (Author abstract) (47 Refs)

37. NONSELECTIVE EXPRESSION OF SIMIAN VIRUS 40 LARGE TUMOR ANTIGEN FRAGMENTS IN MOUSE CELLS.

Reddy VB, Tevethia SS, Tevethia MJ, Weissman SM
Southern Medical and Pharmaceutical Corporation, 3500 East Fletcher Ave., Tampa, FL, 33612

Proc Natl Acad Sci USA; 79(6,part1):2064-2067 1982

To understand the role of various functional domains of simian virus 40 early tumor antigens, we have cloned and introduced into mouse cells portions of early simian virus 40 DNA. Two types of truncated large tumor antigen (33 and 12.3 kilodaltons), as well as small tumor antigen, were identified by immunoprecipitation. Both truncated large tumor antigens have been found to be overproduced with respect to the small tumor antigen, although the 12.3-kilodalton truncated large tumor antigen was more stable than the 33-kilodalton one. Nonviral 53-kilodalton protein was not found associated with either truncated large tumor antigen in immunoprecipitations. (Author abstract) (34 Refs)

TUMOR ASSOCIATED TRANSPLANTATION ANTIGENS

38. CHARACTERIZATION OF TUMOR-ASSOCIATED ANTIGEN FROM HUMAN CARCINOMA OF THE UTERINE CERVIX.

Nadkarni JJ, Satam MN, Damle SR, Rajpal RM, Nadkarni JS
Immunology Div., Cancer Res. Inst., Parel, Bombay 400012, India

Gynecol Oncol; 13(2):175-183 1982

In vitro demonstration of cell-mediated immune responses to tumor-associated antigen (TAA) was observed with autologous tumor extracts from patients with cervical cancer. Seventy-six percent of these patients exhibited an inhibitory effect with autologous antigens while 59% reacted with homologous antigens. A progressive rise in percentage inhibitory activity was associated with increasing stage of the disease. The physicochemical and immunochemical characterization of the TAA found on the membrane of cervical tumor cells suggested that it may be a lipid-protein complex containing an enzyme having immunological determinants such as those of term-placental alkaline phosphatase enzyme. (Author abstract) (24 Refs)

39. INCREASED OR DECREASED IMMUNOGENICITY OF TUMOR-ASSOCIATED ANTIGEN ACCORDING TO THE AMOUNT OF VIRUS-ASSOCIATED ANTIGEN IN RAT TUMOR CELLS INFECTED WITH FRIEND VIRUS.

Yamaguchi H, Moriuchi T, Hosokawa M, Kobayashi H
Lab. Pathology, Cancer Inst., Hokkaido Univ. Sch. Medicine, Kita-15, Nishi-7, Kita-ku, Sapporo 060, Japan

Cancer Immunol Immunother; 12(2):119-123 1982

Grading of tumor-associated antigen (TAA) is described with particular reference to the amount of virus-associated antigen (VAA) newly produced by non-lytic virus infection. Complement-dependent cytotoxic sensitivity of Friend virus (FV)-KMT-17 rat fibrosarcoma cells to anti-VAA serum increased proportionally following serial passage generations with a max at passage 6. The absorbing capacity potentials for removing 50% of anti-VAA serum activity were 12.0x higher in FV-KMT-17 (F6), and 3.2x higher in FV-KMT-17 (F4) cells than in FV-KMT-17 (F2) cells. No difference in absorbing capacities of FV-KMT-17 (F0, 2, 4, and 6) for anti-TAA serum were observed. When WKA/Hok rats were immunized with FV-KMT-17 (F2, 4, 6 and 0) cells having various amounts of VAA and subsequently challenged with 10(5) or 10(6) viable KMT-17 cells, survival rates of 20.8%, 83.3%, 18.2% and 45.8%,respectively, were obtained. Immunization of FV-tolerant rats with FV-KMT-17 (F2, 4, and 6) cells resulted in similar levels of transplantation resistance without marked difference from the non-passage F0. Immunization of normal rats with a mixture of WLFT-6 rat thymoma cells [1.6 x 10(7) possessing an amount of VAA almost equivalent to that in FV-KMT-17 (F4)] and 5.0 x 10(7) KMT-17 cells resulted in lower transplantation resistance than for FV-KMT-17 (F4) cells alone, suggesting that VAA and TAA must be present on the same cell. The results indicated that TAA immunogenicity increases when an appropriate amount of VAA is expressed on the tumor cell surface and decreases when a relatively low or excessive amount of VAA is expressed. (22 Refs)

CLINICAL DIAGNOSTIC STUDIES

40. PHASE I TRIALS OF MURINE MONOCLONAL ANTIBODIES TO TUMOR ASSOCIATED ANTIGENS: PRELIMINARY OBSERVATIONS.

Dillman RO, Sobol RE, Royston I

Dept. Medicine, Univ. California, San Diego, CA, 92161

Protides Biol Fluid Proc Colloq; 29:915-920 1982

Murine monoclonal antibodies (MoAbs) to tumor-associated antigens were infused into two patients with chronic lymphocytic leukemia (CLL) and two melanoma patients with advanced malignancies refractive to standard therapy. Prior to treatment, MoAb reactivity was confirmed in vitro with the patients' CLL cells or melanoma tissue. T101, an IgG2A produced by immunizations with T cell leukemia line 8402, was given to one CLL patient at doses of 1 and 3 mg on successive days then 12 mg 2 wk later, and a single 10 mg dose was given to the other CLL patient. Both melanoma patients were given single 10 mg infusions of M225, an IgGa2 produced by immunization with the M21 melanoma cell line. In circulating CLL cells, after infusion of T101, there was an immediate, marked decrease in lymphocyte number that reached a max in 2 hr, then rapidly increased. Serum MoAb had disappeared from circulation by 4 hr. Since T65 antigen persisted throughout the test period, no significant antigen modulation associated with leukemia cell recovery occurred. In melanoma patients, while no in vivo binding to tumor was demonstrated, M225 levels were still detectable 24 hr after infusion. Significant systemic reactions occurred with 10 and 12 mg infusions of T101; all resolved after administration of fluids and epinephrine. (17 Refs)

41. EPSTEIN-BARR-VIRUS-SPECIFIC T-CELL MEMORY IN RENAL-ALLOGRAFT RECIPIENTS UNDER LONG-TERM IMMUNOSUPPRESSION.

Gaston JS, Rickinson AB, Epstein MA

(c/o Epstein)Dept. Pathology, Univ. Bristol Medical Sch., Univ. Walk, Bristol BS8 1TD, England

Lancet; 1(8278):923-925 1982

The level of long-term responsiveness of cytotoxic T cells to Epstein-Barr (EB) virus has been measured in peripheral-blood mononuclear-cell cultures from symptom-free renal-allograft recipients under conventional immunosuppression. Eight of 22 patients showed a profoundly impaired responsiveness when compared with healthy control donors. The allograft recipients as a group showed raised antibody titers to EB-virus capsid and early antigens, but within the group there was no clear relation between these antibody titers and the level of EB-virus-specific cytotoxic-T-cell function. These findings are particularly relevant to the pathogenesis of the malignant lymphomas to which renal-allograft recipients are unusually susceptible, in view of the evidence implicating EB virus. (Author abstract) (28 Refs)

42. SERA FROM PATIENTS WITH UNDIFFERENTIATED NASOPHARYNGEAL CARCINOMA CONTAIN A FACTOR WHICH ABROGATES SPECIFIC EPSTEIN-BARR VIRUS ANTIGEN-INDUCED LYMPHOCYTE RESPONSE.

Sundar SK, Ablashi DV, Kamaraju LS, Levine PH, Faggioni A, Armstrong GR, Pearson GR, Krueger GR, Hewetson JF, Bertram G, Sesterhenn K, Menezes J

(c/o Menezes) Lab. Immunovirology, Pediatric Res. Center, St. Justine Hosp., 3175 Cote St. Catherine, Montreal (Quebec) H3T 1C5, Canada

Int J Cancer; 29(4):407-412 1982

A unique association of Epstein-Barr virus (EBV) with the undifferentiated nasopharyngeal carcinoma (NPC) is a well acknowledged phenomenon. We report here the detection of a factor present in the sera of NPC patients which inhibits the blastogenic response of lymphocytes from EBV seropositive individuals to EB virions or soluble antigens. This lymphocyte-stimulation inhibitor (LSI) was found to be associated with the IgA fraction of the serum immunoglobulins. No inhibitory activity was detected in the sera and their immunoglobulin fractions from healthy (both EBV-seropositive and seronegative) individuals and patients with other carcinomas of the head and neck region. Interestingly, the IgA-LSI was absent in the sera of NPC patients who were successfully treated and remained in remission, while it was readily detectable in the sera of NPC patients in relapse. LSI-positive IgA fractions did not inhibit mitogenic response of lymphocytes to phytohemagglutinin. Taken together, the data presented suggest that LSI is a specific inhibitor of the response of sensitized lymphocytes to EBV antigens and that it may indeed represent a marker of great clinical significance regarding undifferentiated nasopharyngeal carcinoma, particularly for its prognosis. (Author abstract) (36 Refs)

43. DIFFERENTIAL LOSS OF T LYMPHOCYTE MARKERS IN ADVANCED CUTANEOUS T CELL LYMPHOMA.

Holden CA, Staughton RC, Campbell MA, MacDonald DM

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J Am Acad Dermatol; 6(4,part1):507-513 1982

Tumor biopsies from a 71-yr-old man with disseminated cutaneous T-cell lymphoma (CTCL) was assayed for T-cell markers. The patients showed multiple cutaneous tumors, hepatomegaly, lymphadenopathy, and early bone marrow involvement. The CTCL cells contained antigens reacting with antisera to human T-lymphocyte antigen and a monoclonal antiserum (OKT3), but has lost their RBC rosetting capacities and acid alpha-naphthyl acetate esterase (ANAE) activity. The CTCL cells did not express antigens associated with helper or suppressor T-cells (identified using OKT4 and OKT8 antisera, respectively). The use of monoclonal antisera against T-cell surface antigens may eventually provide antigenic profiles of the malignant cells present in CTCL of differing degrees of aggressiveness, leading to more accurate prognoses and earlier recognition and treatment. (19 Refs)

44. IMMUNOLOGIC CHARACTERIZATION OF A HELPER T-CELL LYMPHOMA.

Gramatzki M, Dolan MF, Fauci AS, Maples JA, Bonnard GD, Strong DM
(c/o Strong) Tissue Bank, Naval Medical Res. Inst., Bethesda, MD, 20814
Blood; 59(4):702-708 1982

The lymphocytes of a patient with a T-cell non-Hodgkin's lymphoma with peripheral blood involvement and polyclonal hypergammaglobulinemia were characterized in terms of surface markers and immunologic functions. Using the fluorescence-activated cell sorter and employing various monoclonal antibodies against T-cell surface antigens, it was shown that almost all of the patient's peripheral blood lymphocytes were positive for OKT4 and 9.3, antibodies that recognize helper T-cell subset. The circulating lymphoma cells had typical characteristics for T cells; they formed spontaneous rosettes with sheep erythrocytes and stained with the pan T-cell antibodies 9.6 and 10.2, but did not react with other anti-T-cell monoclonal reagents such as OKT3, UCHT-1, and 3A1. The cells appeared to be mature by the fact that they did not stain with OKT6, and terminal deoxynucleotidyl transferase was undetectable. Functionally, they were able to provide 'help' for antibody production, and they could be stimulated to produce moderate amounts of interleukin-2, while unable to proliferate in response to mitogens. Morphologically, some of the lymphocytes showed a deeply cleaved nucleus. (Author abstract) (53 Refs)

45. ACUTE LYMPHOCYTIC LEUKEMIA: BIOLOGICAL MARKERS OF CLINICAL RESPONSE.

Mauer AM, Bowman WP, Dow LW, Look AT, Williams D
St. Jude Children's Res. Hosp., Memphis, TN, 38101
J Cell Physiol; Suppl1:127-132 1982

New biological observations that have clinical importance in the treatment of acute lymphoblastic leukemia (ALL) are presented, and current therapeutic problems are described. One hundred and thirty-five patients were entered into the treatment program for standard-risk patients; 101 had WBC counts less than 25,000/cubic mm (mm3) and none of those patients have relapsed. Nine of 34 patients with counts greater than 25,000/mm3 have already relapsed. Proliferative activity was assessed by determining the tritiated thymidine labeling index of blood and bone marrow leukemic blast cells. A significant difference in treatment outcome was found when the group of patients was divided into two parts based on higher or lower level of proliferative activity in the blood and bone marrow blast cells. Bone marrow treatment failed in 42% of patients with labeling index (LI) less than 6%, and in 74% of patients with LI greater than 6%. Initial blast cell karyotypes of 135 patients with ALL were analyzed. The patients with greater than 50 chromosomes have had only two treatment failures. Only 70% of 28 patients with pseudodiploid karyotypes achieved initial remission and 19 have experienced treatment failure. Leukemic blast cell DNA content was analyzed by flow microfluorometry and the data was correlated with the results of the cell surface marker studies. Cells having hyperdiploid DNA content were more likely to have an expression of surface common ALL antigen. However, those cells having T-lymphocyte markers rarely have abnormal DNA content detectable by flow cytometry. These observations suggest the existence of an interrelationship among studied biological features associated with treatment response. (12 Refs)

46. 'TARGET' CELLS, CELLULAR PHENOTYPES, AND LINEAGE FIDELITY IN HUMAN LEUKAEMIA.

Greaves MF
Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England
J Cell Physiol; Suppl1:113-125 1982

Features of leukemic phenotypes in relation to normal hemopoietic differentiation were investigated in a study developed as a part of a routine immunodiagnostic service for leukemia in the United Kingdom (UK). Leukemic samples (heparinized blood, lymph node biopsies, cerebrospinal fluid, and peritoneal aspirates) were obtained from referring hospitals throughout the UK. A presumptive normal sequence of antigen (and other marker) expression in T cell differentiation is presented. The scheme is based upon reported antigenic heterogeneity of cortical and medullary thymocytes and subsets of blood T cells. The corresponding maturation 'positions' of 95 leukemic T cell phenotypes analyzed are presented. T-acute lymphoblastic leukemia (T-ALL), and T-non-Hodgkin's lymphoma in childhood 'correspond' to early or late thymocyte populations while T cell leukemias or lymphomas of older (greater than 35 yr) patients diagnosed as cutaneous lymphoma or leukemia, chronic lymphocytic leukemia, prolymphoblastic leukemia, or lymphoblastic lymphoma, all had 'mature' T phenotypes. The phenotypes that were documented in non-T-ALL are summarized. The majority of complementary ALL that do not synthesize detectable mu chain nevertheless have rearranged mu chain genes as revealed by molecular hybridization studies. Alterations in phenotype during leukemia progression or relapse may provide some evidence for distortion of 'normal' genetic programs as well as revealing the lineage affiliations of various clonogenic populations. Alterations in the latter population may indirectly indicate the possible target cell population involved. (89 Refs)

47. EVALUATION OF METHODS OF DETECTING TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE IN HUMAN HEMATOLOGIC MALIGNANCIES. COMPARISON OF IMMUNOFLUORESCENCE AND ENZYMATIC ASSAYS.

Cibull ML, Coleman MS, Nelson O, Hutton JJ, Gordon D, Bollum FJ
Dept. Pathology, Univ. Kentucky, Lexington, KY, 40536
Am J Clin Pathol; 77(4):420-423 1982

Terminal transferase (TdT) activity and antigen have been measured in 267 specimens of human bone marrow and peripheral blood by using a biochemical assay for enzymatic activity and an immunofluorescence test for antigen. Oligo p(dA)50 and dGTP were used as reagents in the biochemical assay and either rabbit anti-calf TdT or rabbit anti-human TdT was used as the primary antibody for immunofluorescence. Because both false-positive and false-negative detection of TdT antigen occurs, the biochemical assay of TdT activity is considered the standard against which immunofluorescence assays must be measured. If specimens of cells contained TdT activity, then the immunofluorescence detected antigen in 91% of cases (rabbit anti-calf TdT) and 95% of cases (rabbit anti-human TdT). When no TdT activity was detected, the immunofluorescence test was positive in 7.8% of cases (rabbit anti-calf TdT) and 5.2% of cases (rabbit anti-human TdT). When air-dried slides were shipped by air mail to a distant location before being stained for immunofluorescence, TdT antigen was detected in only 33% of matched pair cases which contained TdT activity. From this study, the authors conclude that with current methodology, immunofluorescence tests for TdT antigen must be carried out on slides prepared in the testing laboratory and that such tests are reliable in more than 90% of cases. However, because a small percentage of results are false positives and false negatives, the authors suggest that if a patient's clinical response is not consistent with the immunofluorescence TdT result, an enzymatic assay for TdT activity be carried out. (Author abstract) (19 Refs)

48. MEMBRANE MARKER STUDIES WITH ANTI-T, ANTI-IA (DR) AND ANTI-MYELOBLAST ANTISERA IN ACUTE LEUKAEMIAS.

Lebacq AM, Goffinet P, De Bruyere M, Rodhain J, Sokal G
Unite de Recherches sur les Maladies du Sang, Clos Chapelle-aux Champs 30, UCL 3052, 1200 Brussels, Belgium
Eur J Cancer Clin Oncol; 18(2):147-153 1982

Hetero-antisera reacting specifically with all cells of the T lineage, with Ia-like (DR) antigens or with myeloblasts were used as diagnostic aids in the classification of 64 acute leukemias. The anti-myeloblast proved particularly useful in discriminating early myeloblasts from atypical lymphoblasts and undifferentiated blasts. (Author abstract) (23 Refs)

49. CYTOTOXIC ANTIBODY REACTIVITY IN SERA OF MELANOMA PATIENTS AGAINST ALLOGENEIC AND AUTOLOGOUS CULTURED TUMOR CELLS AND FIBROBLASTS.

Brown JM, Shoffner PC, Tondreau SP, Matthews EJ, Terry WD, Rosenberg SA
Div. Surgical Oncology, Univ. Illinois Medical Center, 840 South Wood, Chicago, IL, 60612
Cancer Res; 42(6):2216-2222 1982

Using a complement-dependent microcytotoxicity assay, sera from melanoma patients were analyzed for antibody reactivity with cultured melanoma and normal adult skin fibroblasts. Sera from Stage I tumor-bearing patients prior to surgical excision, poor-prognosis Stage I and Stage II patients after tumor excision and lymphadenectomy but prior to adjuvant therapy, and normal individuals with a similar age and sex distribution were tested against a melanoma-fibroblast pair from an allogeneic donor. The groups displayed a wide range of cytotoxicity against both cell types, and no serum possessed melanoma-specific reactivity. Mean cytotoxicity of the Stage I tumor-bearing group was not significantly different (p greater than 0.05) from that of the normal group for either target cell, and patients whose tumors went on to recur were not different from nonrecurrent patients. The Stage I and II postlymphadenectomy patients were not different from the normals in fibroblast reactivity. However, melanoma reactivity was significantly higher in the postlymphadenectomy patients than the normals (p less than 0.02). This was the result of an elevated reactivity in the patient population who remained disease free compared to patients whose tumors went on to recur (p less than 0.01), although a large overlap existed between these two groups. Cytotoxicity against autologous melanoma and fibroblasts was observed with sera obtained throughout the clinical course of four Stage II patients, and no melanoma-specific reactivity was detected. Absorption with cultured fetal fibroblasts of sera from Stage II patients both before and after immunotherapy with Bacillus Calmette-Guerin and allogeneic melanoma removed reactivity against allogeneic and autologous melanoma and adult fibroblasts. Therefore, the predominant antibody reactivity detected in these patients was directed against common fetal fibroblast-associated antigen, and no evidence was obtained for the presence of antibodies reactive with unique or shared tumor-specific antigens. (Author abstract) (35 Refs)

50. THE EVOLUTION, IMPLICATIONS, AND APPLICATIONS OF THE HEPATITIS B VACCINE.

Alter HJ
NIH, Bethesda, MD
JAMA; 247(16):2272-2275 1982

One aspect of hepatitis B vaccine is that it might serve indirectly as the first cancer vaccine because of the possible relationship between hepatitis B virus (HBV) infection and primary hepatocellular carcinoma (HCC). Evidence for causality is summarized. The global distribution of hepatitis B surface antigen (HBsAg) carriers and HCC are almost identical. (14 Refs)

51. PRESENCE OF HEPATITIS B SURFACE ANTIGEN BEFORE PRIMARY HEPATOCELLULAR CARCINOMA.

Nomura A, Stemmermann GN, Wasnich RD
Japan-Hawaii Cancer Study, Kuakini Medical Center, 347 N Kuakini St., Honolulu, HI, 96817
JAMA; 247(16):2247-2249 1982

In a study of 7,498 men of Japanese ancestry in Hawaii, 18 incident cases of primary hepatocellular carcinoma were identified after a follow-up period of 13 yr. Sixteen of the 18 patients had stored serum specimens available for analysis. Ten of the 16 had positive serum test results for hepatitis B surface antigen in their original specimens. None of 48 matched control subjects, whose stored serum specimens were also analyzed, had similar positive test results. This finding indicates that hepatitis B surface antigenemia preceded primary hepatocellular carcinoma in many patients. (Author abstract) (20 Refs)

52. BREAST CANCER SKIN TEST ANTIGENS OF INCREASED SENSITIVITY PREPARED FROM VESICULAR STOMATITIS VIRUS-INFECTED TUMOR CELLS.

Austin FC, Boone CW, Levin DL, Cavins JA, Djerassi I, Rosner D, Case R, Klein E
NCI, NIH, Westwood Building, Room 10A07, Bethesda, MD, 20205
Cancer; 49(10):2034-2042 1982

Crude membrane (CM) extracts were prepared from five cultured breast tumor lines (MDA-MB-157, MDA-MB-231, ZR75-1, HSO578T, and MCF-7) which had been infected with vesicular stomatitis virus (VSV) to augment their antigenicity. In skin test trials, CM extracts of uninfected MCF-7 cells elicited positive responses in 0 of 13 (0%) tests in breast cancer patients, while VSV-MCF-7 elicited positive responses in 11 of the same 13 patients (84.6%). CM extracts of VSV-ZR75-1 and VSV-MCF-7 elicited greater delayed hypersensitivity responses (mm induration at 48 hr) in breast cancer patients than in patients with lung carcinoma or melanoma. Although the sensitivity of VSV-ZR75-1 was too low (10 of 28, or 35.7%, of tests positive) to be useful as a skin test antigen, VSV-MCF-7 elicited positive responses in 30 of 38 (78.9%) tests in breast cancer patients, as compared to 2 of 15 (13.3%) and 2 of 13 (15.4%) of tests in patients with lung carcinoma and melanoma, respectively. The 'virus-augmented' CM extract of cultured MCF-7 cells exhibited markedly greater sensitivity as compared to control MCF-7 extracts (p less than .005), with a high degree of specificity for breast cancer patients as compared to patients with the other neoplasms (p less than .00001). The results of skin testing with VSV-MCF-7 CM extracts demonstrated antigenic cross-reactivity with a large number of breast cancer patients, a finding of great importance for any potential immunotherapy and/or immunodiagnosis. (Author abstract) (27 Refs)

OTHER RELATED STUDIES

53. NEWER METHODS OF CANCER TREATMENT: SECTION 1. IMMUNOTHERAPY.

Terry WD, Hodes RJ
Immunology Branch, NCI, Bethesda, MD
Cancer - Principles and Practice of Oncology. DeVita VT, Hellman S, and Rosenberg SA, ed. Philadelphia, Lippincott, 1926 pp., 1982.

Discussions relative to immunotherapy center around history, therapeutic agents, clinical trials, and conclusions. Immunotherapy is still in the early stages of development as a cancer treatment. A few facts seem to be established: that the development of delayed hypersensitivity reactions in a tumor leads to tumor necrosis; that id or iv BCG administration slightly prolongs remissions and causes a somewhat longer prolongation of post-relapse survival time in patients with acute myelogenous leukemia; that BCG treatment reduces the frequency of recurrences of papillary carcinoma of the bladder; and that levamisole may be a useful treatment for several types of cancer. The slow progress of clinical immunotherapy is related to the very large number of potential variables in the host-tumor-therapy interaction, which in turn has meant that the development of immunotherapy remains empirical. Additional information on the surface antigens of tumor cells, immune system-tumor cell interactions, and the regulation and control of immunologic function must be obtained before rational decisions can be made on the basis of the probability that immunotherapy will be useful in the systemic treatment of cancer. (235 Refs)

54. HUMAN PLASMACYTOMA WITH AN UNUSUAL KARYOTYPE GROWING IN VITRO AND PRODUCING LIGHT-CHAIN IMMUNOGLOBULIN.

Karpas A, Fischer P, Swirsky D
Dept. Haematological Medicine, Cambridge Univ. Clinical Sch., Cambridge, England
Lancet; 1(8278):931-933 1982

A new human plasmacytoma line (Karpas 707) was established from the cells of the bone-marrow and peripheral blood of a patient with Bence-Jones-positive multiple myeloma. The cells of this new line resembled the patient's malignant cells and fresh myeloma cells from nine other patients in being Epstein-Barr viral nuclear antigen negative. They looked like plasma cells and they secreted only lambda light chains. Both these cells and the patient's fresh cells were hypodiploid and contained the Philadelphia chromosome and several other markers. This line seems to be the first human plasmacytoma line since the IgE lambda-producing line (U266) established in 1968, and it may be suitable for the production of human monoclonal antibodies. (Author abstract) (14 Refs)

55. A HUMAN PLASMA CELL LINE: INDUCTION AND CHARACTERIZATION.

Miller CH, Carbonell A, Peng R, Paglieroni T, MacKenzie MR
Dept. Pathology, Sch. Medicine, Univ. California, MS-1, Room 3453, Davis, CA. 95616
Cancer; 49(10):2091-2096 1982

A stable line of IgG K producing human plasma cells was established from a myelomatous human bone marrow using conditioned media from a rapidly metabolizing lymphoblast line, RPMI 4098. Growth in RPMI 1640 (15% fetal calf serum) at 6% CO2 promoted a 62-hr doubling time with a preferred cell concentration of 1 x 10(6)/mL. Surface marker studies showed: no receptors for sheep erythrocytes, no surface immunoglobulins, variable number of cells bearing complement receptors and 83% bearing Fc receptors. Although transmission electron micrographs demonstrated a poorly developed endoplasmic reticulum, radioimmunoassay showed 23 ng IgG and 28.7 ng Kappa were produced by 1 x 10(6) cells in 72 hr. Further, the cells are lipase, esterase and Epstein-Barr nuclear antigen negative. ASG banding showed a total chromosome number that varied from 46-49. Since the number of human plasma cell lines is limited, it is felt that this line will augment the immunobiological study of human myeloma. (Author abstract) (16 Refs)

56. ESTABLISHMENT AND CHARACTERIZATION OF HUMAN NEUROBLASTOMA AND GANGLIONEUROBLASTOMA CELL LINES.

Morrison LJ, Cochran AJ, Gibson AA, Willoughby ML, More IA
Dept. Pathology and Surgery, Univ. California Los Angeles Center for Health Sciences, Los Angeles, CA, 90024
Br J Cancer; 45(4):531-542 1982

The establishment in culture and characterization of four human neuroblastoma (NB) cell lines and one human ganglioneuroblastoma cell line are described. Each cell line fulfilled at least two of four criteria for malignant or transformed cells: viz, subcultured more than 70x, high saturation density with absence of contact inhibition, population-doubling time within a range of 10-40 hr, and tumor formation in nu/nu mice. Each cell line also fulfilled at least two of three criteria for neuroblastoma cells: viz, humoral and cell-mediated immune reactivity toward NB-associated cell-surface antigen, intracellular storage and extra-cellular secretion of catecholamines, and characteristic neuroblast and ganglion-cell morphology. (Author abstract) (22 Refs)

57. ANTIGENICITIES OF MUCINS - THEIR RELEVANCE TO TUMOUR ASSOCIATED AND STAGE SPECIFIC EMBRYONIC ANTIGENS.

Feizi T
Applied Immunochemistry Res. Group, Div. Communicable Diseases, Clinical Res. Centre, Harrow, Middlesex, England
Adv Exp Med Biol; 144:29-37 1982

Differentiation antigens expressed in secreted glycoproteins are reviewed. Secreted glycoproteins have provided fundamental information on the nature of the major blood group antigens and their precursors. Blood group branched (I) and linear antigens are expressed on type 2 precursor chains; the expression of I antigen of 'Ma type' in gastric mucins is genetically determined. Changes in antigenicity of gastric mucosal glycoproteins associated with cancer are discussed. Mucins could serve as valuable sources of oligosaccharide haptens of differentiation antigens. (17 Refs)

58. PRODUCTION OF MONOCLONAL ANTIBODIES AGAINST MYCOPLASMA HYORHINIS AS A SECONDARY EFFECT OF IMMUNISATION OF MICE WITH CULTURED CELL LINES.

Vennegoor C, Polak-Vogelzang AA, Hekman A
Netherlands Cancer Inst., Amsterdam, The Netherlands

Protides Biol Fluid Proc Colloq; 29:759-762 1982

Melanoma cell line Sk-Mel-25 and acute lymphoblastic leukemia line CCRF-CEM were used to immunize Balb/c mice for preparation of monoclonal antibodies against human tumor cell surface antigens. Antibodies were detected by binding of 125I-F(ab')2 anti-mouse IgG. While the hybridomas were selected because their antibodies reacted preferentially with tumor cells, it was found that the antibodies produced were specific for Mycoplasma hyorhinis. With a combination of the indirect immunofluorescence test with monoclonal antibody and DNA staining with Hoechst 33258, the reaction against mycoplasm may be visualized. (8 Refs)

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Tumor-Associated Antigens

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DETECTION/ CHARACTERIZATION/ ISOLATION

1. HEPATITIS B VIRUS AND PRIMARY LIVER CANCER: DEMONSTRATION OF A CYTOPLASMIC TUMOR ANTIGEN IN THE TRANSFORMED HEPATOCYTE.

Romet-Lemonne JL, Barin F, Goudeau A, Maupas P
Institut de Virologie de Tours, Facultes de Medecine et de Pharmacie, 2bis, Boulevard Tonnelle, 37000 Tours, France

C R Acad Sci [III] (Paris); 294(1):9-14 1982

The presence of tumor antigen was studied in human hepatoma cell line PLC/PRF/5 by indirect immunofluorescence and immunoperoxidase assay using antisera from 14 Senegalese patients with primary hepatocellular carcinomas. Ten of the 14 sera were HBs Ag-positive, 4/10 also HBe Ag-positive, 3/14 anti-HBsd antibody-positive and 1/14 anti-HBc antibody-positive. Twenty-two sera without hepatitis B virus markers from African Blood donors and from cancer patients were used as controls. Tumor antigen (HBV/T) was found in the cytoplasm of the human hepatoma cells. The same antigen was also detected in primary hepatocellular carcinoma tissues. The data obtained with serum and tissue controls indicate that the

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HBV/T Ag-anti-HBV/T system seems to be associated with the transformation of hepatocytes by hepatitis B virus. (15 Refs) (In FRE)

2. PHENOTYPING HUMAN LEUKEMIC T-CELL LINES: ENZYME MARKERS, SURFACE ANTIGENS AND CYTOGENETICS.

Martin PJ, Giblett ER, Hansen JA
Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
Immunogenetics; 15(4):385-398 1982

We have compared phenotypic markers for a series of established human leukemic T-cell lines collected from different laboratories. Cell lines were tested first for genetic markers using polymorphic enzymes and then for expression of T lymphoid cell surface differentiation antigens using monoclonal antibodies. Chromosomal analysis was used as an additional method for identification of selected cell lines. On the basis of enzyme markers, it was possible to assign each of the cell lines examined to one of nine different groups. With two exceptions, surface antigen phenotypes for each of 12 cell lines were clearly distinctive. Thus, some groups of cell lines indistinguishable by enzyme markers could be further subdivided by surface antigen phenotyping. However, significant quantitative variation in expression of individual antigens was observed. In addition, surface antigen expression was not uniform in different subcultures of one cell line studied in detail. These results indicate that leukemic T-cell lines cannot be used generally as simple models of surface antigen expression in normal T-cell differentiation. (Author abstract) (38 Refs)

3. EXPRESSION IN LARGE AMOUNTS OF BOTH I-A AND I-E ANTIGENS ON THE MURINE B-CELL LEUKEMIA, BCL1.

Letarte M, Meghji G, Lorimer G
Div. Immunology, Res. Inst., Hosp. Sick Children, 555 University Ave., Toronto M5G 1X8, Canada
Mol Immunol; 19(4):557-564 1982

The level of Ia antigens present on a murine B cell leukemia, passaged in BALb/c mice and designated BCL1, was measured in the cellular radioimmunoassay. Leukemic cells obtained from spleens of mice inoculated 4 wk previously with the tumor were shown to express, on a per cell basis, 14x more Ia than control BALB/c spleen cells. The wet wt of a leukemic spleen was approx 18x more than that of a control spleen. Several preparations yielded, on the av, 110x more Ia per leukemic mouse spleen than per control spleen. This augmentation suggests that BCL1 leukemic spleens are an abundant source for the purification of murine Ia antigens. Contrary to a previous report, I-Ad antigens could be demonstrated on BCL1 cells. Ib cells, which do not express I-E antigens on their surface shared with BCL1 cells Ia specificities recognized by A-TH anti-A-TL serum. Furthermore a monoclonal antibody to Ia-15-like specificity of I-A subregion was reactive with BCL1 cells. I-Ed antigens, as reported previously, were also present on BCL1 cells: 0.7 x 10(6) molecules of RAM-Fc were bound per BCL1 cell incubated with either of two independently derived monoclonal antibodies to Ia-7-like specificity. Immunoprecipitation of 125I-labeled Ia enriched fractions with either A-TH anti-A-TL serum or with monoclonal antibodies directed at I-Ad or I-Ed antigens yielded a major radioactive band of mol wt 28,000 under non-reducing conditions and of mol wt 34,000 under reducing conditions. (Author abstract) (26 Refs)

4. SEROLOGICAL ANALYSIS OF CELL SURFACE ANTIGENS ON METHYLCHOLANTHRENE-INDUCED MOUSE SARCOMAS WITH ANTISERA PRODUCED AGAINST THE TUMORS.

Tanimoto M, Takahashi T, Nishizuka Y
(c/o Takahashi) Lab. Experimental Pathology, Aichi Cancer Center Res. Inst., Tashiro-cho, Chikusa-ku, Nagoya 464, Japan
Gan; 73(2):184-192 1982

Out of nine cell lines from methylcholanthrene-induced fibrosarcomas in BALB/c, four lines without expression of murine leukemia virus (MuLV) were selected for immunization of three different F1 hybrids with mitomycin C-treated in vivo sarcoma cells. Antibody activity was tested by immune adherence (IA) and protein A (PA) assays after the eighth immunization. Two sarcomas, CMC-11 and CMC-12, produced antibodies detectable by IA in (BALB/c x C3H/He)F1, but no antibodies were detected by PA. (BALB/c x C3H/He)F1 anti-CMC-11 was tested against CMC-11 and three other MuLV-sarcomas as well as against the skin fibroblast (C-11) from a BALB/c mouse, in which the primary CMC-11 sarcoma was induced. CMC-11 line reacted up to 1/80, but other lines were weakly positive or negative. Absorption analysis showed that the antigen defined by anti-CMC-11 was present on CMC-11 as well as on many other sarcoma cell lines, but not on BALB/c thymocytes and spleen cells, nor on leukemia and myeloma cells. Among five fibroblast cultures tested, C-14 showed complete absorption. It seems significant that only C-14 produced tumor nodules in BALB/c mice, in contrast to four other fibroblast cultures. This suggested that this antibody was directed against antigens present on transformed fibroblasts and sarcoma cells. The specificity of (BALB/c x C3H/He)F1 anti-CMC-12 serum indicated that this antiserum also seemed to detect transformation-related antigens, although it showed a broader specificity with regard to the tissue representation detected. (Author abstract) (29 Refs)

5. DIFFERENT EXPRESSION OF LYT DIFFERENTIATION ANTIGENS AND CELL SURFACE GLYCOPROTEINS BY A MURINE T LYMPHOMA LINE AND ITS HIGHLY METASTATIC VARIANT.

Altevogt P, Kurnick JT, Kimura AK, Bosslet K, Schirrmacher V
Institut fur Immunologie und Genetik, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, D-6900 Heidelberg, W. Germany
Eur J Immunol; 12(4):300-307 1982

Cloned lines of the methylcholanthrene-induced DBA/2 T lymphoma Eb and its highly metastatic variant line ESb were analyzed for differences in the expression of serologically detectable cell surface differentiation markers. Flow cytofluorographic analysis of cells stained with fluorescein isothiocyanate-conjugated monoclonal rat anti-mouse Thy-1, Lyt-1, Lyt-2 and complement-dependent cytotoxicity with mouse alloantisera against Lyt-3.2 and Ly-6.2 revealed, for the parental low metastasizing line, Eb, a phenotype of Thy-1+, Lyt-1-, Lyt-3+, Ly-6+, whereas the highly metastasizing variant line typed as Thy-1-, Lyt-1+, Lyt-2-, Lyt-3-, Lyt-6-. Analysis of galactose oxidase/NaB3H4-labeled glycoproteins from Eb and ESb clones by polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulfate showed further phenotypic differences. Selective binding of radiolabeled glycoproteins to Helix pomatia or Vicia villosa-Sepharose, respectively, allowed the identification of T130 to be expressed on Eb cells and T145 to be expressed on some ESb clones. The latter antigen is expressed on murine cytotoxic T lymphocytes. Immune precipitation analysis revealed that Eb and ESb bear different molecular forms of the T200 antigen. Comparisons of iodinated surface proteins derived from tumor cells either treated or untreated with tunicamycin indicated that many of the differences in membrane proteins between Eb and ESb cells could be attributed to differences in glycosylation. Our results, derived from a defined tumor system of lymphoid origin, show that the progression from a low to a high malignant tumor line can be associated with changes in the expression of various defined cell surface differentiation antigens. The question of a possible relationship between tumor progression and cell differentiation or dedifferentiation is discussed. (Author abstract) (47 Refs)

6. EVIDENCE OF A PHOSPHORYLATED PROTEIN SPECIFIC OF HUMAN COLON CARCINOMA CELLS.

Munsch N, Raux H, Fondaneche MC, Burtin P
Inst. de Recherches Scientifiques sur le Cancer, B.P. 8, 94802 Villejuif Cedex, France
Biochem Biophys Res Commun; 106(1):87-93 1982

Two human tumor cell lines, HT29 and Caco2, and the mammary tumor cell line MDA -MB-231 synthesize in culture a 42 kilodalton (42K) protein detectable by immunoprecipitation. This protein, which is phosphorylated in the two colon tumor cell lines, is not detectable by antisera against normal adult colon, suggesting that the 42K protein represents a tumor specific antigen. Addition of a differentiating agent, retinoic acid, reduces the growth of the tumor cells by 50%, but has no effect on the expression of the 42K protein. (10 Refs)

7. IDENTIFICATION OF CYTOKERATIN ANTIGENS IN NOVIKOFF ASCITES HEPATOMA.

Schmidt WN, Pardue RL, Tutt MC, Briggs RC, Brinkley BR, Hnilica LS
Dept. Biochemistry, A.B. Hancock Jr. Memorial Lab., Vanderbilt Univ. Cancer Center, Vanderbilt Univ. Sch. Medicine, Nashville, TN, 37232
Proc Natl Acad Sci USA; 79(10,part1):3138-3142 1982

Further characterization of three polypeptide antigens present in Novikoff ascites hepatoma (mol wt 39,000, 49,000, and 56,000-p39, p49, and p56, respectively), has established the identity of these proteins as cytokeratins. Two-dimensional gel electrophoresis revealed that each of the three proteins exists in several isoelectric forms, all characteristic of the keratins. The antigens p39 and p56 had amino acid compositions compatible with this family of proteins, and immunofluorescence microscopy localized the antigens on elaborate filament arrays indicative of the cytokeratins. Antibodies monospecific for the p39 antigen, purified by using affinity chromatography, were used to demonstrate that protein p39 was specific for Novikoff hepatoma cells. These results suggest that the cytokeratins contain cell-specific species that can be useful as markers for differentiation and neoplasia. (Author abstract) (50 Refs)

8. THE MDCK EPITHELIAL CELL LINE EXPRESSES A CELL SURFACE ANTIGEN OF THE KIDNEY DISTAL TUBULE.

Herzlinger DA, Easton TG, Ojakian GK
Dept. Anatomy and Cell Biology, State Univ. New York, Downstate Medical Center, Brooklyn, NY, 11203
J Cell Biol; 93(2):269-277 1982

Monoclonal antibodies were prepared against the Madin-Darby canine kidney (MDCK) cell line to identify epithelial cell surface macromolecules involved in renal function. Lymphocyte hybrids were generated by fusing P3U-1 myeloma cells with spleen cells from a C3H mouse immunized with MDCK cells. Hybridomas secreting anti-MDCK antibodies were obtained and clonal lines isolated in soft agarose. We are reporting on one hybridoma line that secretes a monoclonal antibody that binds to MDCK cells at levels 20-fold greater than background binding. Indirect immunofluorescence microscopy was utilized to study the distribution of antibody binding on MDCK cells and on frozen sections of dog kidney and several nonrenal tissues. In the kidney the fluorescence staining pattern demonstrates that the antibody recognizes an antigenic determinant that is expressed only on the epithelial cells of the thick ascending limb of Henle's loop and the distal convoluted tubule and appears to be localized on the basolateral plasma membrane. This antigen also has a unique distribution in nonrenal tissues and can only be detected on cells known to be active in transepithelial ion movements. These results indicate the probable distal tubule origin of MDCK and suggest that the monoclonal antibody recognizes a cell surface antigen involved in physiological functions unique to the kidney distal tubule and transporting epithelia of nonrenal tissues. (Author abstract) (62 Refs)

9. AVIDIN-BIOTIN IMMUNOENZYMATIC DETECTION OF TUMOR ASSOCIATED ANTIGENS UTILIZING HYBRIDOMAS (MEETING ABSTRACT)

Whitmore KE, DeKernion JB, Fahey JL, Messing EM, Bubbers JE
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

The supernatants of hybridomas resulting from the fusion of spleen cells from mice immunized with the human bladder cancer cell line 647V and mouse myeloma line SP2/OAg14, were used to detect tumor associated antigens (TAA's) on human cell lines, (melanoma, lung carcinoma, and normal lymphocytes), and fresh frozen tissue sections of normal and malignant bladder, utilizing a modification of Hsu's ABC immunoperoxidase assay. The avidin-biotin-peroxidase complex (ABC) is a 2-step immunoenzyme assay that bridges the test sample, primary antibody or hydridoma, secondary antibody (biotinylated horse antimouse IgG), and the avidin molecule of the ABC complex. When compared to the immunofluorescent, radioimmunoassay, and other immunoenzymatic assays, (peroxidase-anti-peroxidase), increased sensitivity and decreased background staining are achieved. The use of positive controls. (normal human lymphocytes and normal fresh frozen bladder tissue), emphasized the importance of the following variables: antigen accessibility, section fixation, concentration of the secondary antibody, (increased concentration provides increased biotinylated antibody sites to bind ABC complex avidin molecules), and incubation time of the oxidizing staining reagent, 3-3' diaminobenzidine (DAB). The ABC immunoenzymatic assay allows for: greater dilution of the primary antibody, labelling of the secondary antibody, and an excessive number of ABC complex binding sites. (no Refs)

10. SIMULTANEOUS DETERMINATION OF T-ANTIGEN AND ABO CELL SURFACE ANTIGENS IN TRANSITIONAL CELL CARCINOMA (MEETING ABSTRACT)

Kidd D, Javadpour N, Fourcroy J, O'Connel K
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

The purpose of this study was to investigate the changes in cell surface antigens which result in the interruption of communication and interaction through the cell surface membrane. These changes reflect an alteration in the genome which modifies the biosynthetic pathways of the Golgi apparatus. The demonstration of T-antigen expression in breast carcinoma and the loss of blood group iso-antigens in invasive transitional cell carcinoma prompted inquiry into the correlation between the carbohydrate precursor of the human blood system MN and the epithelial surface blood group isoantigens. A red cell adherence assay to detect T-antigen on deparafinized slides of transitional cell carcinoma of the bladder was developed. Peanut agglutinin which has anti-T properties as well as other nonspecific binding sites is layered over the slides, washed, then covered with neuraminidase treated red cells. Red cell adherence was noted on areas of the bladder tumor that binds plant lectin. This was compared with the specific red cell adherence (SRCA) for ABO antigen on the same tissue samples. Of the 17 patients, 14 demonstrated loss of their cell surface ABO antigens. Of the 14, 28% demonstrated expression of the T-antigen. This would imply that T-antigens may be complementary to A, B, O, Ag in predicting potential malignancies of bladder cancer when the conventional histologic examination can not provide any prediction. (no Refs)

11. MELANOMA ASSOCIATED GLYCOPROTEINS DEFINED BY MONOCLONAL ANTIBODIES (MEETING ABSTRACT)

Reisfeld RA, Bumol TF
Scripps Clinic and Research Foundation, 10666 No. Torrey Pines Road, La Jolla, CA, 92037
Hybridoma; 1(2):184 1982

Monoclonal antibody 9.2.27 has been used in biosynthetic enzymatic and structural studies to define an antigenic complex on human melanoma cells that consist of an N-linked glycoprotein (Mr 250,000) and a high molecular weight proteoglycan (HMW-C) with an Mr greater than 480,000. Pulse-chase biosynthetic analyses of the 250K glycoprotein indicated Endoglycosidase H-sensitive precursors. Biosynthesis of the HMW-C coincides with Endoglycosidase H resistance of the 250K glycoprotein and is inhibited by exposure of the melanoma cells to the ionophore monensin. Biosynthetic structural and enzymatic studies suggest that the 250K component recognized by the 9.2.27 monoclonal antibody is a core glycoprotein of a chondroitin sulfate proteoglycan found both in freshly explanted melanoma tumor tissues and at the surface of cultured melanoma cells. Monoclonal antibody F11 recognizes a glycoprotein of Mr 100,000 (100K) in spent media of melanoma cells and three glycoproteins of Mr 75, 77 and 100K in detergent lysates of these same cells. Pulse-chase analyses indicate recognition of 75/77K molecules by F11 early in the chase in the absence of detectable 100K antigen and the kinetics of this analysis suggest that the 75/77K components may be biosynthetic precursors of the 100K glycoprotein. Treatment of melanoma cells with monensin prevents the biosynthesis of the 100K antigen resulting in the secretion of altered molecular weight species into spent media of melanoma cells. (no Refs)

12. MONOCLONAL ANTIBODY DEFINED GLYCOLIPID ANTIGENS OF HUMAN GASTROINTESTINAL TRACT (MEETING ABSTRACT)

Blaszczyk M, Karlsson KA, Hansson G, Larsson G, Brockhaus M, Herlyn M, Steplewski Z, Koprowski H
University of Goteborg, Goteborg, Sweden
Hybridoma; 1(2):202 1982

From mice immunized with human pancreatic carcinoma cell line four hybridomas secreting monoclonal antibodies specific for B blood group antive glycosphingolipids have been obtained. Three of 4 antibodies reacted selectively with B active blood group glycolipids with Type II chain, one of which did not crossreact with B substances having Type I chain. The forth monoclonal antibody reacted with blood group B active glycolipids with either Type I or Type II chain structure. None of these antibodies displayed any reactivity with nonfucosylated B active glycolipid substance. Four hybridomas secreting monoclonal antibodies specific for Leb antigen were produced by immunization of mice with a human colorectal adenocarcinoma cell line. All four antibodies reacted with Leb glycolipids and the binding was inhibited by lacto-N-difucohexaose, while no inhibition could be detected with lacto-N-tetraose, lacto-N-fucopentaose I and lacto-N-fucopentaose II. Monoclonal antibody produced against human rectal carcinoma cell line did not react with purified blood group glycolipids of known A, B, H, Leb, and Lea, Led and Lec structures. The only substance reactive was alpha1-3 fucosylated paragloboside. Four hybridomas secreting antibodies directed against the same antigen were established after immunization of mice with freshly isolated tumor cells from patients with gastric and pancreatic carcinomas. (no Refs)

13. THE USE OF MONOCLONAL ANTIBODIES FOR THE DETECTION OF HUMAN CONNECTIVE TISSUE DIFFERENTIATION ANTIGENS APPEARING ON SARCOMAS (MEETING ABSTRACT)

Feit C, Bartal AH, Hirshaut Y
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Hybridoma; 1(2):203 1982

Our two preliminary goals were 1) to obtain monoclonal antibodies (mAb) that distinguish sarcomas from carcinoma cell lines, and 2) mAb that differentiate among the various histological types of sarcoma. A malignant fibrohistiocytoma (MFH) and a fibrosarcoma (FS), obtained immediately after surgery were sterilely minced, passed through a fine wire mesh and aliquots were used for immunization of Balb/c mice. P3UI plasmacytoma cells were fused with spleen cells from immunized mice. Supernates from newly formed hybridomas were screened against a human sarcoma and carcinoma cell line. Screening for surface and internal antigens was accomplished using an indirect immunofluorescence assay run against acetone-fixed cells. An enzyme-linked immunosorbent assay was used to detect surface antigens of viable cells. Clones reacting only with sarcoma were subcloned and expanded. Subsequent characterization of mAb consisted of interaction with an expanded panel of human sarcoma, carcinoma and skin fibroblast cell lines. Of 380 clones screened from the MFH fusion, we obtained 2 mAb (VIF3 and VIE4) that reacted with 18/20 and 17/20 sarcomas respectively, but were negative with 7 carcinoma cell lines tested. Both mAb reacted with 4/6 fibroblast cell lines. From the FS fusion, of 840 clones screened, 3 mAb (25E2, 12C9 and 21H5) which were nonreactive with all carcinoma lines tested were positive with 6/12 sarcomas and 1/4 fibroblast lines. This latter group recognizes more restricted mesodermal antigen(s) appearing on sarcomas and connective tissues. (no Refs)

14. EXPRESSION AND DISTRIBUTION OF P69,71 (LEU 1) ON BENIGN AND MALIGNANT HUMAN LYMPHOID CELLS: CORRELATION WITH CONVENTIONAL CELL MARKERS AND WITH MONOCLONAL ANTIBODY OKT1 (MEETING ABSTRACT)

Knowles DM, Halper JP, Wang CY
Departments of Pathology and Medicine, Columbia University, College of Physicians and Surgeons, New York, NY
Lab Invest; 46(1):46A 1982

This study delineates the distribution of a surface antigen complex of 69,000 and 71,000 daltons, p69,71 (Leu 1), on benign and malignant human lymphoid cells by indirect immunofluorescence using a monoclonal antibody. p69,71 expression was correlated with conventional markers and with monoclonal antibody antibody OKT1, which also detects a 69,000-dalton surface protein. Normal peripheral blood, tonsil, spleen, and lymph node T cells were p69,71+ OKT1+, whereas B cells were p69,71+OKT1-. Twenty-two T cell malignancies expressing intrathymic and peripheral phenotypes were p69,71+ OKT1+, and the percentage of positive cells and antigenic density increased with maturation, comparable to normal T cells. The majority of neoplastic cells in 33 of 36 cases of B-CLL, 10 of 15 B small lymphocytic cell lymphomas, and 9 of 29 follicular center cell lymphomas of each surface immunoglobulin isotype, including two cases with an associated monoclonal protein, expressed p69,71 OKT1 was expressed in parallel with p69,71 with respect to percentage of positive cells and antigenic density. Myeloma plasma cells and non-B, non-T ALL cells were p69,71-OKT1-. (no Refs)

15. BIOLOGIC PROFILE OF HUMAN MELANOMA CELL ANTIGENS (MEETING ABSTRACT)

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Department of Pathology, University of California, and Scripps Clinic and Research Foundation, La Jolla, CA
Lab Invest; 46(1):91A 1982

Monoclonal xenoantibodies to a cytoplasmic and to a membrane-bound tumor-associated antigen in human melanoma cells have been produced. Analysis with cultured human cell lines and with surgically removed tumor tissues indicates that the plasma membrane antigen is restricted to melanoma, whereas the cytoplasmic antigen is synthesized by tumor cells of various histologic types. The membrane-bound antigen, is an efficient target of antibody-mediated lysis of melanoma cells. The cytoplasmic antigen which consists of four glycopolypeptides of 94,000, 75,000, 70,000, and 25 daltons, is readily shed by tumor cell lines into the spent culture medium. Human melanoma cells have also unexpectedly been found to express Ia-like antigens. Melanoma derived Ia-like antigens are immunologically functional. Monoclonal antibodies have also been produced to these antigens. The level of Ia-like antigens on melanoma cells is significantly lower than on B lymphoid cells, and this is likely to reflect a reduced synthesis more than an increased shedding. Melanoma cell-derived Ia-like antigens have a structure similar to that of B lymphoid cell-derived Ia-like antigens. The antigens are composed of two noncovalently associated glycoproteins. One chain, the alpha chain, has an approximate molecular weight of 34,000 and the other one, the beta chain, has an approximate molecular weight of 29,000. We have studied benign and malignant melanocytic skin lesions with our monoclonal antibody to Ia-like antigens and have found that the expression of Ia-like antigens is restricted to malignant melanoma. (no Refs)

16. HUMAN NEUTROPHIL FCGAMMA RECEPTOR DISTRIBUTION AND STRUCTURE.

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Dept. Cellular Physiology and Immunology, Rockefeller Univ., New York, NY, 10021
Proc Natl Acad Sci USA; 79(10,part1):3275-3279 1982

Fc receptors (FcR) for IgG on human cells were analyzed with two monoclonal antibodies, 3G8 and 4F7. Fab fragments of both hybridoma IgGs inhibited binding to neutrophils of soluble rabbit IgG complexes and sheep erythrocytes (E) coated with rabbit IgG. The number of sites for 3G8 Fab was 135,000 per neutrophil, roughly equivalent to the number of sites for rabbit IgG in immune complexes (112,000 per cell). We did not observe human IgG1 binding sites on neutrophils, although binding of IgG1 to FcR-bearing lines U937 and HL-60 was readily demonstrated. Other cell types bearing 3G8 binding sites were mature chronic myelogenous leukemia cells, eosinophils, 6% of E-rosetting lymphocytes, and 15% of Ig-bearing peripheral lymphocytes. No binding of 3G8 Fab was observed on the FcR-bearing cell lines U937, HL-60, Raji, Daudi, and K562 or on blood monocytes. However, 15% of monocytes cultured for 7 days and 60% of lung macrophages expressed 3G8 antigen. When analyzed by sodium dodecyl sulfate/polyacrylamide gel electrophoresis, the neutrophil FcR immunoprecipitated with 3G8 or 4F7 Fab-Sepharose displayed a broad band extending from Mr 73,000 to 51,000; in many experiments this band was resolved into two poorly separated components, centered at Mr 66,000 and 53,000. These results show that human neutrophil FcR for IgG is different from that on monocytes, with respect to both antigenic composition and binding of monomeric IgG1. (Author abstract) (35 Refs)

17. MOLECULAR CHARACTERIZATION OF PREIMPLANTATION EMBRYONIC SURFACE ANTIGENS WITH AN ANTITERATOCARCINOMA SERUM (MEETING ABSTRACT)

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Anat Rec; 202(3):12A 1982

Cell surface antigens expressed by preimplantation mouse embryos and teratocarcinomas are studied using a rabbit antiserum (A-N1) against clonally derived nullipotential mouse teratocarcinoma stem cells (Nulli-SCC-1). Indirect immunofluorescen studies indicate that following absorption with adult mouse tissue, A-N1 recognizes surface antigens on all preimplantation stage mouse embryos including blastocyst trophectoderm and inner cell mass. N1 antigens are also found on the female germ line but not male. Development is inhibited when mouse embryos are cultured in the presence of A-N1 serum suggesting a possible developmental role for the antigens detected. In vivo absorption of A-N1 in adult male or female mice does not remove all A-N1 activity suggesting one or more antigens detected are embryo specific. Using Staphylococcus aureus mediated immunoprecipitation followed by 1-D and 2-D electrophoresis, we have identified 7 protein or glycoprotein antigens which are specifically precipitated from embryos and teratocarcinoma cells (TC) with A-N1. Differential absorption of A-N1 with whole live TC cells vs detergent lysate of TC cells has permitted the differentiation between cell surface and cytoplasmic antigens. Four of the 7 precipitated are cell surface antigens with approximate molecular weights of 16,000, 18,000, 37,000 and 60,000 and appear on both mouse blastocysts and nullipotential TC cells. Precipitation with in vivo absorbed A-N1 is being used to determine which of these antigens is embryo specific. (1 Ref)

18. SPECIFICITY AND TUMOR LOCALIZATION OF A MONCLONAL ANTIBODY (MA) DEFINING A HUMAN GLIOMA ASSOCIATED EXTRACELLULAR MATRIX ANTIGEN (MEETING ABSTRACT)

Bourdon MA, Wikstrand CJ, Coleman RE, Bigner DD

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Abstracts of the 58th Annual Meeting, June 11-13, 1982, Philadelphia, Pennsylvania. American Association of Neuropathologists 386 pp., 1981.

We have used MA81C6, generated against the glial fibrillary acidic protein positive human glioma cell line U-251MG, to examine the distribution and localization of a glioma-mesenchymal extracellular membrane, but not normal brain. Cell line and tissue specificities were assayed by cell surface radioimmunoassay (RIA), absorption analysis, and peroxidase-antiperoxidase (PAP) immunohistology. 131-I-MA81C6 tumor localization in U-251M6 nude mouse xenografts was examined by radioscintigraphy. MA81C6 specificity analysis showed that GMEM was present in extracellular matrix (ECM) of glioma cell lines (14/16), glioma xenografts (7/9), and proliferative endothelial basement membranes of GBM (10/11). GMEM was also expressed by cells of mesenchymal origin including sarcoma (2/6) and fibroblast (8/9) cell lines and ECM of liver and spleen sinusoids and kidney medulla. GMEM was not detected in adult and fetal brain, muscle, skin, meningiomas, medulloblastoma, and astrocytomas (5/6) examined. By RIA and PAP, MA81C6 did not cross-react with fibronectin, laminin or collagen types I-V. 131-I-MA81C6 tumor localization in U-251MG-bearing nude mice showed specific MA81C6 localization in the glioma xenografts; in paired labeled experiments using a 125-I-labeled control immunoglobulin, tumors were clearly imaged by 131-I-radioscintigraphy within 48 hrs. (no Refs)

19. THE SURGICAL MANAGEMENT OF PRIMARY CARCINOMA OF THE LIVER.

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World J Surg; 6(1):66-75 1982

Results of liver resection for primary hepatic carcinoma performed on 165/935 patients are reported. Hepatitis B surface antigen (HBsAg) was present in 78.4% of 328 tested patients. Surgical resection was contraindicated in intractable ascites, a delay greater than 10% at 45 min of the Bromosulphalein excretion test, and albumin below 3 g/100 ml. It is recommended that arteriograms be performed before resection. Technetium-99m scanning, hepatic angiography, computed tomography, and peritoneoscopy were useful in detecting and delineating tumor. Operative techniques discussed include abdominal exploration, left lateral segmental resection, left hemihepatectomy, left medial segmental resection, right hemihepatectomy, extended right hepatectomy, right subsegmentectomy, resection for ruptured hepatoma, and hepatic dearterialization. Complications occurred in 68 patients, 33 of whom died. An operative mortality rate of 20% was achieved. Median survival rate 10 mo compared to 1.1 mo for patients not treated by resection. Five yr survival was 20%, with one patient alive at 20 yr. (10 Refs)

IMMUNOLOGICAL STUDIES

20. IMMUNOGENICITY AND AMPLIFIER CELL PRODUCTION BY TUMOR VACCINES ENHANCED BY CONCANAVALIN A.

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Gan; 73(2):193-205 1982

The induction of immune resistance to L1210 murine leukemia by three types of L1210 vaccines was compared under conditions in which in vitro cell proliferation and transplantability to mice were completely suppressed. L1210 cells treated with glutaraldehyde plus concanavalin A (ConA) were more potent in inducing antitumor immunity than those treated with Vibrio cholerae neuraminidase or mitomycin C (MMC). This and the finding that cell-bound ConA enhanced the immunogenic potency of MMC- or formaldehyde-treated L1210 vaccine indicate that ConA endowed the cells with additional potency in inducing antibody immunity. ConA-free and ConA-bound vaccine cells took up the same amount of anti-L1210 antibody, suggesting that cell-bound ConA did not increase tumor-associated antigen molecules on the tumor cell surface. However, adoptively transferred spleen cells of mice sensitized with ConA-bound, but not ConA-free, vaccine amplified the vaccine-induced antitumor immunity in the recipients. These donor spleen cells suppressed the in vitro proliferation of live L1210 cells no more than non-primed spleen cells, nor was their amplifying activity abrogated by treatment with anti-Lyt-2.1 antibody and rabbit sera as a source of complement. This indicated that cytotoxic T cells and/or their precursors were not involved in the observed amplification. This as well as the finding that their amplifying activity was completely abrogated by treatment with rabbit anti-mouse brain-associated T cell antigen antisera and rabbit sera as a source of complement, led us to conclude that amplifier T cell production, associated with vaccine-bound ConA, was responsible for the enhanced immunogenic potency of ConA-bound vaccines. (Author abstract) (17 Refs)

21. IMMUNOLOGICAL LOCALIZATION OF PRIMARY TUMORS.

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Chirurg; 53(4):258-262 1982

Specificity of cellular immune reactions was studied in 115 cancer patients. Antigens were prepared by KCl extraction of tissues from bronchial carcinoma (BC), gastric carcinoma (GC), mammary carcinoma (MC), and colorectal carcinomas (CRC) of varying histological differentiation. Lymphocytes were prepared from venous blood of 115 cancer patients, 25 patients with precancerous conditions (mastopathy of Prechtel Stages II and III), and 54 clinically healthy controls. Lymphocyte-antigen reactions were measured using the electrophoretic mobility test. Encephalitogenic factor was used as a nonspecific antigen. Specific reaction patterns were observed for each type of tumor antigen (TA). Lymphocytes from cancer patients (CL) reacted most strongly with TA from the corresponding tumor type. BC-CL reacted with BC-TA in 31/35 tests. GC-CL reacted with GC-TA in 25/26 tests. MC-CL reacted with MC-TA in 16/18 tests. CRC-CL reacted with CRC-TA in 31/36 tests. Reactions with TA of other types were weak or negative. Lymphocytes from healthy controls were unreactive in 139/158 tests. Specificity of lymphocytic reactivity is potentially useful as a diagnostic aid. (19 Refs) (In GER)

22. COMBINED IMMUNOLOGICAL AND HISTOCHEMICAL ANALYSIS OF SKIN AND LYMPH NODE LESIONS IN HISTIOCYTOSIS X.

Thomas JA, Janossy G, Chilosi M, Pritchard J, Pincott JR

Dept. Histopathology, Royal Marsden Hosp., Sutton, Surrey, England

J Clin Pathol; 35(3):327-337 1982

The immunological phenotype of the cells involved in skin and lymph node lesions from two cases of histiocytosis X (H-X) were analyzed by immunofluorescence techniques using combinations of heterologous and monoclonal antisera to Ia-like antigen and human cortical thymocyte (HTA-1) determinants. These cells were also characterized by a new technique using simultaneous immunofluorescence and enzyme histochemistry for acid phosphatase (ACPase). The major cell type in the lesions was found to express the same Ia+, HTA-1+ phenotype as normal epidermal Langerhans' cells (LC) and was unreactive for ACPase. Additional cell types included Ia-, HTA-1-multinucleate giant cells and residual lymphoid populations These findings endorse previous concepts that H-X is a proliferation of abnormal LC and emphasize the heterogeneous nature of the cells involved in the disease. (Author abstract) (31 Refs)

23. ANTIGEN SPECIFICITY OF SQUAMOUS CANCERS OF THE HEAD AND NECK BASED ON TUMOR SITE USING THE SLIDE LEUKOCYTE ADHERENCE INHIBITION ASSAY.

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J Surg Oncol; 20(1):41-45 1982

Patients with a diagnosis of squamous cancer of the upper aerodigestive (UAD) system were tested with extracts of squamous cancer arising from several regions of the UAD tract and compared to various control populations, using the slide leukocyte adherence inhibition (LAI) assay. Seven tumor extracts were tested. Twenty-five of 77 tests (32%) were positive in unselected UAD squamous cancer patients. However, matching patients with tumor extract by the site of origin within the UAD tract, 19 of 22 tests (86%) were positive when the site of origin was identical for leukocyte donor and extract. Two of four patients tested with an extract prepared from a different site within the same region of the UAD system were positive; whereas only 4 of 51 tests (8%) were positive in patients tested with an extract from a cancer arising from a different region within the UAD tract (F less than 0.001). One of 33 tests using patients with either no cancer (11 tests), squamous cancer of other regions (15), or adenocarcinoma (7) reacted to the extracts of UAD tract cancers. We conclude that patients with squamous cancer of the UAD tract can recognize distinct tumor-associated antigens that are site-specific and are non-cross-reactive using the LAI technique. (Author abstract) (17 Refs)

24. MONOCLONAL ANTIBODIES TO TUMOR ASSOCIATED ANTIGENS (TAAS) ON TRANSITIONAL CELL CARCINOMA (TCC) (MEETING ABSTRACT)

Messing EM, Bubbers JE, Whitmore KE, DeKernion JB, Fahey JL

No affiliation given

77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association Missouri. American Urological Association 254 pp., 1982.

Murine monoclonal antibodies were separated to antigens on human TCC cells by fusion of spleen cells from mice recently immunized with TCC cells, with a non-secreting syngeneic myeloma cell line. Several such fusions have been performed. Immunoglobulin secreting hybrid cells which are immortalized and cloned have thus been created, so as to provide unlimited amounts of monospecific antibodies. Hybridoma supernatants have been screened for desired immunologic reactivity with: a) the immunizing cell line, b) other TCC cell lines, and c) malignant human cell lines of non-TCC origin, using a solid phase radioimmunoassay. Twenty-nine hybridomas produced antibodies to the immunizing lines: of these, 4 recognized calf serum (CS) or CS dependent antigens, 5 recognized common tissue antigens, and 16, while not reacting with all non-TCC cells, recognized antigens which failed to display the restricted expression expected of TAA. Four antibodies, however, were considered to be directed toward TCC TAAs since they recognized TCC cells only or most TCC cell lines and not more than 2 of 6 malignant non-TCC cells. Antibody 2E1-F3 which reacts with only (and all tested) TCC targets, was chosen for futher study. Quantitative absorptions of these antibodies with a panel of non-malignant homogenized tissue, (4 different organs from each of 4 patients) failed to reduce the ability of these antibodies to bind with TCC target cells, thus demonstrating that they did not react with normal human tissue. (no Refs)

25. SPECIFICITY OF AUTO-TUMOR CYTOTOXICITY EXERTED BY FRESH, ACTIVATED AND PROPAGATED HUMAN T LYMPHOCYTES.

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Int J Cancer; 29(5):547-553 1982

The specificity of auto-tumor cytotoxicity exerted by patients T lymphocytes was investigated. Lymphocytes were used as effectors against freshly separated tumor cells. Activation was achieved by treatment with interferon (Hu-IFN-alpha), stimulation with PHA, co-cultivation with autologous tumor biopsy cells (ATS) and allogeneic lymphocytes (MLC). ATS was the most efficient in generating auto-tumor cytoxicity. In some cases the lymphocytes also damaged autologous tumor cells, but IFN-pretreatment of the lymphocytes had no such effect. When the ATS- or MLC-activated lymphocytes were propagated with conditioned medium known to contain Interleukin-2, their lytic potential against autologous tumors was maintained. On the population level, the ATS was specific for the autologous tumor cells. Cold target competition tests suggested that in the MLC-s the autologous tumor cells were killed by a distinct set of lymphocytes because allogenic cells did not compete. Thus, in these cultures the auto-tumor specificity of the lysis was on the level of the effector subset. Therefore, it is likely that, independently of the mode of activation, the auto-tumor lysis is the function of lymphocytes which recognize tumor- or organ-specific antigens on the target cells. (30 Refs)

26. ALTERATIONS IN THE PHENOTYPE OF HAIRY CELLS DURING CULTURE IN THE PRESENCE OF PHA: REQUIREMENT FOR T CELLS.

Worman CP, Beverley PC, Cawley JC
Dept. Haematology, Univ. Coll. Hosp., Grafton Way, London WC1, England
Blood; 59(5):895-899 1982

Culture studies of peripheral blood mononuclear cells from seven entirely typical cases of hairy cell leukemia showed that after culture in the presence of PHA for 2-5 days, the predominant cell type changed from E- SIg+ CIg+ gammaFcR+ muFcR+ hairy cells to an E+ SIg- CIg- gammaFcR- muFcR- population of transformed cells derived from hairy cells. Depletion and readdition experiments demonstrated that cell-to-cell contact with T cells was necessary for the phenotypic change, while several observations indicated that the E+ population was not derived from T cells present before culture. The E positivity of the cultured cells was shown to be due to the possession of E receptor not acquired from the culture fluid, but the cells differed from true T cells in lacking both mature and immature T-cell antigens. The relevance of these in vitro observations to the continuing controversy concerning the nature of the hairy cells and to the in vivo fluctuations in immunologic phenotype not infrequently observed in hairy cell leukemia is briefly discussed. (Author abstract) (23 Refs)

27. ANALYSIS OF IMMUNOSUPPRESSOR CELLS INDUCED BY IMMUNIZATION OF SOLUBILIZED TUMOR-ASSOCIATED ANTIGENS PREPARED FROM A RAT FIBROSARCOMA.

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Dept. Orthopedic Surgery, Sch. Medicine, Hokkaido Univ., Sapporo, Hokkaido, Japan
Nippon Seikeigeka Gakkai Zasshi; 55(8):779-792 1981

Soluble tumor antigens were prepared from chemically-induced rat fibrosarcoma KMT-17 cells by sodium deoxycholate (DOC) extraction. Significant responses detected by the footpad assay and Winn assay were demonstrated in rats immunized with DOC extract. However, rats previously immunized with DOC extract showed a significant enhancement of tumor growth when challenged with KMT-17 cells. This enhancement was specific for the tumor line used. The tumor-neutralizing ability of KMT-17 immune spleen cells was abrogated when DOC extract immune spleen cells were added to a mixture of KMT-17 cells and KMT-17 immune spleen cells. This suppressive activity of the spleen cells was diminished by the treatment with anti T serum and complement. After fractionation of DOC extract immune spleen cells by the Ficoll density gradient, the cells in the light layer showed an enhancing effect on tumor growth, whereas the cells in the heavier region of the gradient had an inhibiting effect. These results suggested that both immunosuppressor cells and cytotoxic cells were induced in rats immunized with DOC extract. (Author abstract) (29 Refs)

28. DIFFERENTIAL ANTIBODY RESPONSE AMONG MOUSE STRAINS TO GUINEA PIG LEUKEMIA CELL SURFACE ANTIGENS AND ACTIN (MEETING ABSTRACT)

Dingle S, Akeson R, Lessard JL
Children's Hospital Research Foundation, Cincinnati, OH, 45229
Hybridoma; 1(2):197 1982

We have carried out a study to optimize the production of hybridoma antibodies to two different types of antigens, cell surface components and cytoplasmic proteins, by comparing the immune response of five mouse strains or hybrids to guinea pig leukemia cell surface antigens and cardiac actin. Six-ten females from the SJL, C57Bl/6, CB6F1/J, Balb/C and C3H/He strains were used in each set. In the case of actin, the mice were given subcutaneous injections of about 20 ug of bovine cardiac actin on day 0 (in Freund's complete adjuvant), 14 and 28 (in incomplete adjuvant); an intravenous injection was administered on day 42. Test bleeds were taken on day 0, 21, 35 and 49. There was a great deal of variability in individual responses. The CB6F1/J mice showed the highest titers at day 21 but the Balb/C strain showed the best titer at day 49. Nine of the ten SJL animals expired from apparent anaphylaxis upon the IV injection at day 42. However, the single remaining animal showed the highest titer that we observed. In the case of guinea pig leukemia cells, the mice were immunized with 5x10(6) EN-L2C cells on days 0, 14, 28 and 42 along with 300 ug poly (I) poly (C). Test bleeds were taken one week after each boost. Antibody was estimated using a 125I-protein A solid phase assay with intact EN-L2C cells attached to poly-L-lysine coated plates. SJL mice showed a significantly higher titer of antibody at all test bleeds. The remaining four strains all showed similar but somewhat lower titers except for the C3H mice which had an average signal/noise ratio of 24 on day 49. (no Refs)

VIRUS ASSOCIATED ANTIGENS

29. EVIDENCE FOR TWO FUNCTIONALLY DISTINCT CROSS-REACTIVE TUMOR ANTIGENS ASSOCIATED WITH ULTRAVIOLET LIGHT AND CHEMICALLY INDUCED TUMORS.

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Transplantation; 33(4):352-360 1982

Experiments were conducted to determine the distribution and function of common tumor antigens shared by UV light-, benz[a]pyrene (BP)-, and methylcholanthrene (MCA)-induced tumors. When lymph node cells were removed from UV, BP, or MCA tumor-immune mice and held in tissue culture for 4 days, a population of cytotoxic T lymphocytes (CTLs) emerged that were capable of lysing a battery of different tumor targets. These CTLs displayed crossreactive in vivo activity in Winn-type assays. These CTLs recognized tumor-associated antigens (TAAs) common to both UV and chemically induced tumors. These common TAAs were incapable of eliciting cross-protective tumor immunity when tumor immunizations and challenges were made entirely in vivo. The state of cross-protective immunity within hyperimmune mice is directed toward shared tumor-associated transplantation antigens (TA-TAs). These particular determinants are related to the induction etiology of the tumor. Previous reports have suggested that the suppressor T lymphocytes (Ts cells) present in UV-treated animals possess functional specificity for the common TATAs expressed by UV tumors. We believe that UV-induced Ts cells recognize the common TAAs shared by UV and MCA tumors. Collectively, these data define at least two different classes of common tumor antigens expressed by UV and chemically induced tumors. These antigenic determinants are functionally defined as the TATAs and the common TAAs. The shared TATA function in vivo as rejection antigens and are restricted to tumors induced by the same carcinogenic agent. In contrast, the common TAAs shared by UV and chemically induced tumors are not only recognized by CTLs but more importantly function as immunoregulatory determinants. The importance of these common tumor antigens in host-tumor interactions is discussed. (32 Refs)

30. IDENTIFICATION OF AN ANTIGEN ASSOCIATED WITH TRANSFORMING GENES OF HUMAN AND MOUSE MAMMARY CARCINOMAS.

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Proc Natl Acad Sci USA; 79(10,part1):3315-3319 1982

Sera from tumor-bearing mice immunoprecipitated an 86,000-dalton glycoprotein from extracts of NIH cells transformed by human mammary carcinoma DNA. This antigen was not immunoprecipitated from extracts of NIH 3T3 cells, spontaneously transformed NIH cells, NIH cells transformed by normal human DNA, NIH cells transformed by human bladder carcinoma DNA, or NIH cells transformed by Rous sarcoma virus DNA. In addition, sera from mice bearing tumors induced by NIH cells transformed by either normal human DNA or human bladder carcinoma DNA did not immunoprecipitate this antigen from extracts of NIH cells transformed by human mammary carcinoma DNA. However, this antigen was immunoprecipitated by sera from mice bearing tumors induced by NIH cells transformed by mouse mammary carcinoma DNAs and from mice bearing primary mammary carcinomas. These results indicate that this glycoprotein represents an antigen that is specifically associated with expression of the transmissible transforming genes of human and mouse mammary carcinomas. (Author abstract) (15 Refs)

31. FREQUENCY AND DISTRIBUTION OF PAPILLOMAVIRUS STRUCTURAL ANTIGENS IN VERRUCAE, MULTIPLE PAPILLOMAS, AND CONDYLOMATA OF THE ORAL CAVITY.

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Am J Pathol; 107(2):212-218 1982

Sixty-seven proliferous squamous epithelial lesions of the oral cavity were examined for the presence of human papillomavirus whole (structural) virion antigens by a peroxidase-antiperoxidase technique having immunospecificity against genus-specific (common) antigens of the papillomaviruses. A positive reaction for papillomavirus genus specific antigens was found in 18 of 29 verrucae, 2 of 5 multiple papillomas, and 3 of 5 condylomata; common antigens were not detected in 28 keratoacanthomas. The positive reaction was invariably intranuclear in cells having a focal or diffuse distribution in the superficial epithelium. This study shows that a variety of squamous epithelial lesions of the mucosa are associated with human papillomaviruses and suggests that these viruses may play an important role in the etiology of some cases of squamous hyperplasia of the oral cavity. (Author abstract) (24 Refs)

32. FREQUENCY AND DISTRIBUTION OF PAPILLOMAVIRUS ANTIGENS IN CERVICAL DYSPLASIA AND CARCINOMA IN SITU (MEETING ABSTRACT)

Kurman RJ, Lancaster WD, Jenson AB

Department of Pathology and Obstetrics and Gynecology, Georgetown University Hospital, Washington, DC

Lab Invest; 46(1):46A 1982

Two hundred and ninety-three cases of cervical dysplasia (139 mild, 72 moderate, 44 severe) and carcinoma in situ (CIS) (38) retrieved from the surgical pathology files of Georgetown University Hospital from 1974 to 1977, were screened for the presence of papillomavirus (PV) antigens, using a peroxidase-antiperoxidase technique, having immunospecificity against the genus-specific (common) antigens of the papillomaviruses on formalin-fixed paraffin-embedded tissue. A positive reaction for PV antigens was found in 68 mild dysplasias, 13 moderate dysplasias, six severe dysplasias, and three CIS. Positive cells were focally or less commonly diffusely distributed in the superficial and intermediate layers of the epithelium in areas of mild or moderate dysplasia and also associated with or immediately adjacent to areas of severe dysplasia and CIS. The positive reaction, invariably intranuclear, was present in nuclei with wrinkled nuclear membranes that were rounded, ovoid, or flattened. Positive cells with flat or ovoid nuclei were mononuclear with scant cytoplasm, whereas those with rounded nuclei were sometimes binucleate and characteristically contained clear cytoplasm. Cells with similar morphologic features to those showing a positive reaction of PV antigens were frequently negative but were also considered as showing wart virus atypia. Cells showing wart virus atypia, irrespective of being PV-positive or negative, were found in 126 mild dysplasias, 51 moderate dysplasias, 24 severe dysplasias, and 10 CIS. (0 Refs)

33. PURIFICATION OF A NATIVE MEMBRANE-ASSOCIATED ADENOVIRUS TUMOR ANTIGEN.

Persson H, Katze MG, Philipson L

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J Virol; 42(3):905-917 1982

A 15,000-dalton protein was purified from HeLa cells infected with adenovirus Type 2. Proteins solubilized from a membrane fraction of lytically infected cells was used as the starting material for purification. Subsequent purification steps involved lentil-lectin, phosphocellulose, hydroxyapatite, DEAE-cellulose, and aminohexyl-Sepharose chromatographies. A monospecific antiserum, raised against the purified protein, immunoprecipitated a 15,000-dalton protein encoded in early-region E1B (E1B/15K protein) of the adenovirus Type 2 DNA. Tryptic finger print analysis revealed that the purified protein was identical to the E1B/15K protein encoded in the transforming part of the viral genome. The antiserum immunoprecipitated the E1B/15K protein from a variety of viral transformed cell lines isolated from humans, rats, or hamsters. The E1B/15K protein was associated with the membrane fraction of both lytically and virus-transformed cell lines and could only be released by detergent treatment. Furthermore, an 11,000-to 12,000-dalton protein that could be precipitated with the anti-E1B/15K serum was recovered from membranes treated with trypsin or proteinase K, suggesting that a major part of the E1B/15K protein is protected in membrane vesicles. Translation of early viral mRNA in a cell-free system, supplemented with rough microsomes, showed that this protein was associated with the membrane fraction also in vitro. (Author abstract) (47 Refs)

34. DEPENDENCE OF TUMOR-FORMING CAPACITIES OF CELLS TRANSFORMED BY RECOMBINANTS BETWEEN ADENOVIRUS TYPES 5 AND 12 ON EXPRESSION OF EARLY REGION 1.

Shiroki K, Maruyama K, Saito I, Fukui Y, Yazaki K, Shimojo H
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J Virol; 42(2):708-718 1982

Recombinants between an adenovirus Type 5 (Ad5) deletion mutant and the Ad12 DNA fragment containing early Region 1 (E1) were isolated from cells cotransfected with the EcoRI-C fragments of Ad12DNA and Ad5 dl312 (deletion in E1A) DNA (rcA) and from cells cotransfected with the SalI-C fragment of Ad12 DNA and Ad5 dl312 DNA (rcB). No recombinant was isolated from cells cotransfected with Ad5 dl313 (deletion in E1B) DNA and restriction fragments of Ad12 DNA. Both rcA and rcB are defective and able to replicate in human embryo kidney (HEK) and KB cells with complementation by dl312. Both rcA and rcB formed Ad12 T antigen g, but not T antigen f, in infected HEK and KB cells. In rcA- and rcB-infected cells, Ad5 E1B and Ad12 E1A genes are transcribed. Heteroduplex and size analysis of rcA-1 or rcB-1 DNA fragments hybridized with Ad12 DNA revealed that rcA-1 DNA has a deletion between 5 and 15 map units with an insertion of a portion of Ad12 DNA (10%) and that rcB-1 DNA has a deletion between 70 and 80 map units with an insertion of a portion of Ad12 DNA (10%). The transformed cell lines, RCAY and RCBY, were established after infection of rat 3Y1 cells with rcA and rcB, respectively. Both Ad5 and Ad12 DNA sequences are contained in these cells. In RCAY cells, Ad12 T antigen g is detected, but Ad12 T antigen f is not. In RCBY cells, both Ad12 T antigens g and f are detected. Only the Ad12 E1A gene is transcribed in RCAY cells, whereas Ad5 E1B, Ad12 E1A, and Ad12 E1B genes are transcribed in RCBY cells. In soft-agar cultures, RCBY cells form large colonies, whereas RCAY cells form only tiny colonies. RCBY cells form tumors as efficiently as 12WY cells in transplanted rats. RCAY cells formed tumors inefficiently. Ad5-transformed 5WY cells do not form tumors. These observations indicate that the efficient tumor formation by RCBY cells is dependent on the expression of the Ad12 E1A and E1B genes, whereas the inefficient tumor formation by RCAY cells is due to the expression of only the Ad12 E1A gene. (Author abstract) (28 Refs)

35. SUPPRESSION OF SPONTANEOUS MAMMARY TUMORIGENESIS DESPITE MTV-1 GENE EXPRESSION IN HYBRID AND BACKCROSS C3H-AVYFB X C3H/SM MICE.

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Lab. Molecular Biology, NCI, Bethesda, MD, 20205
Int J Cancer; 29(5):591-598 1982

Mouse mammary tumor virus (MMTV)-specific RNA and antigen content of normal and neoplastic mouse mammary tissue were measured in strains C3H/Sm and C3H-AvyfB in C3H-AvyfB female x C3H/Sm male F1 hybrids and in (C3H-AvyfB x C3H/Sm) x C3H/Sm male backcross segregants. The molecular data, along with the relative mammary tumor incidences, suggest that the endogenous MMTV provirus expression gene Mtv-1 present in C3H mice is fully expressed in the C3H-AvyfB subline but is silent or more probably absent in the C3H/Sm subline. Cessation of translational expression of endogenous MMTV occurred only in the agouti backcross females, suggesting an association between this phenomenon and the agouti locus of C3H/Sm. Evaluation of the relative MMTV RNA content of nucleic and cytoplasmic fractions from C3H/Sm mammary tissues strongly suggests that transport and/or processing of MMTV RNA is defective in these mice. This defect probably accounts for the absence of detectable MMTV antigens in C3H/Sm and agouti backcross mammary tissues and tumors and may contribute to the observed reduction in mammary tumor incidence. (27 Refs)

36. A RETROVIRUS ASSOCIATED WITH HUMAN ADULT T CELL LEUKEMIA: IN VITRO ACTIVATION.

Hinuma Y, Gotoh Y, Sugamura K, Nagata K, Goto T, Nakai M, Kamada N, Matsumoto T, Kinoshita K
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Gan; 73(2):341-344 1982

Presence of adult T cell leukemia antigen (ATLA) was studied in the mononuclear cell fractions of peripheral blood derived from 11 patients (9 men, 2 women; 48-83 yr old) with adult T cell leukemia (ATL), from a 54-yr-old man with mycosis fungoides (MF), and from 8 healthy adults (6 men, 2 women; 21-44 yr old). The mononuclear cell fractions were cultured in the presence and/or absence of interleukin-2 (IL-2) or T cell growth factor. Some of the fractions were also examined with electron microscopy for virus particles. ATLA positive cells were not detected in any of the cell preparations examined prior to culturing. However, ATLA-bearing cells were observed in the cultures from 6/11 ATL patients and 1/2 ATLA antibody-positive healthy subjects. No ATLA-bearing cells were detected in cultures of one patient with MF and six ATLA antibody-negative healthy subjects. High percentages of ATLA positive cells were found 2-3 days after starting cultures without IL-2; the ATLA were located in the cytoplasm of rather small leukemic cells and were often aggregated. The ATLA-bearing cells in cultures supplemented with IL-2 for a greater than 2 wk were large and often multinuclear with blastoid morphology. Presence of Type C virus particles was observed with electron microscopy in ATL-derived cultures with a high percentage of ATLA positive cells. The results showed that (1) peripheral blood cells of many patients with ATL contain sufficient information for ATLA or ATL virus (ATLV) formation in a repressed form, and suggest that (2) ATLA is associated with ATLV and (3) ATLV is present not only in ATL patients but also in anti-ATLA positive healthy individuals. (6 Refs)

37. THYMIC EPITHELIUM DETERMINES PRELEUKEMIC CELLULAR AND VIROLOGICAL CHANGES IN LEUKEMIA-SUSCEPTIBLE MICE (MEETING ABSTRACT)

Zielinski C, Datta S, Waksal S
Department of Medicine II, University of Vienna, Vienna, Austria
12th Workshop on Leukocyte Cultures, February 14-17, 1982, Vienna, Austria Wiener Medizinische Akademie; :A64 1982

Although leukemia-resistant (AKRxNZB)F1 mice (ANF1) inherit dominant genes for the expression of ecotropic and xenotropic viruses, they do not express these retroviruses on their thymocytes. Prothymocytes of ANF1 did express high levels of retroviruses, however, when they differentiated in the thymi of lethally irradiated leukemia-susceptible AKR mice, but not in other 'low leukemia' strain recipients. Furthermore, prothymocytes of leukemia-resistant ANF1 which had differentiated in grafted irradiated AKR thymi expressed murine leukemia virus antigen and certain surface phenotype changes regarding thymocyte differentiation markers as they were observed to go along with increased murine leukemia virus antigen expression in ANF1 to AKR bone marrow chimeras. No increased murine leukemia virus antigen expression was observed on thymocytes of ANF1 to ANF1 thymus graft chimeras. These experiments suggest that murine leukemia virus antigen expression may occur in a specific thymic environment which further leads to shifts in the expression of thymocyte differentiation markers and finally to the development of leukemia. (no Refs)

38. ISOLATION OF TRANSFORMATION-DEFECTIVE HOST-RANGE MUTANTS OF POLYOMA VIRUS ON NORMAL MOUSE CELLS.

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Virology; 119(2):310-316 1982

Host-range mutants of polyoma virus have been isolated utilizing primary mouse embryo fibroblasts as the permissive host and cells of an established 3T3 line as the nonpermissive host. Five out of five such 'mouse embryo-dependent' (MED) mutants have totally lost transforming ability. Their transformation defects can be complemented by ts-a mutants but not by hr-t mutants. Restriction enzyme digestion shows deletions of 150-200 base pairs in the proximal early region of the viral DNAs (HpaII fragment 4, 79-92 map units). None of the MED mutants produce middle or small tumor antigen species detectable by metabolic labeling and immune precipitation, and none show the middle T-antigen-associated protein kinase activity in vitro. MED mutants are thus indistinguishable from hr-t mutants previously isolated ising polyoma-transformed 3T3 cells as the permissive host. The isolation of nontransforming host-range mutants in the absence of direct polyoma gene complementation confirms a specific prediction of the hypothesis of indirect action by the hr-t gene, according to which the inability to transform must arise concomitantly with the inability to induce a permissive state for virus growth. (Author abstract) (28 Refs)

39. GENETIC ANALYSIS OF TUMORIGENESIS. VIII. SUPPRESSION OF SV40 TRANSFORMATION IN CELL HYBRIDS AND CYTOPLASMIC TRANSFERANTS.

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Cytogenet Cell Genet; 31(4):214-227 1981

Intraspecies somatic cell hybrids of BALB/c mouse 3T3 and SV40-transformed embryonic fibroblast (SVT2) cells were analyzed for transformation-associated properties and their tumorigenic potential in nude mice. In confirmation of our earlier findings, hybrids expressing the viral T-antigen were not suppressed for the ability to clone in medium with 1% serum. In contrast, division rate in medium with 1% and 10% serum, anchorage independence, cytochalasin-sensitive growth control, and tumorigenicity were suppressed noncoordinately, and the extent of suppression varied from one hybrid to another. Suppression was not simply determined by the increased chromosome content of the hybrid cells, nor was suppression correlated with rearrangements of the integrated viral sequence. Similar results were found in cytoplasmic transferants expressing T-antigen. Four independent transferants and subclones derived from them varied in the extent of suppression of anchorage independence and tumorigenicity. In both hybrids and transferents, a low serum requirement for clonal growth apparently was determined solely by expression of SV40 T-antigen, but other transformation properties, as well as tumorigenicity, appeared to require multiple changes in the cellular genome for their expression. These changes must occur during or after viral integration, since they are not expressed in uninfected 3T3 cells. (Author abstract) (47 Refs)

40. DIFFERENT FORMS OF SIMIAN VIRUS 40 LARGE TUMOR ANTIGEN VARYING IN THEIR AFFINITIES FOR DNA.

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J Virol; 42(2):456-466 1982

In various permissive monkey cell lines infected with simian virus 40 there are two major forms of large T antigen which differ in their rate of sedimentation through sucrose gradients. The lighter (5 to 7S) form sedimented slightly more rapidly than the 4S tRNA marker, whereas the heavier (16S) form sedimented slightly more slowly than the 18S rRNA marker. The small t antigen did not form complexes which sedimented as rapidly as those formed by the large T antigen. The 16S T antigen form was converted to the slowly sedimenting 5 to 7S form in the presence of 1.0 M NaCl. The majority of large T antigen synthesized in cell-free protein-synthesizing systems primed by mRNA isolated from infected cells sedimented as the 5 to 7S form even when premixed with excess quantities of cellular T antigen. The formation of the 16S form in infected cells did not require ongoing viral or cellular DNA replication because considerable quantities of this T antigen class were produced in the presence of DNA synthesis inhibitors, such as cytosine cytosine arabinoside. Both 5 to 7S and 16S forms could be isolated separately and, therefore, each could be analyzed as to its individual properties. The 5 to 7S T antigen form bound more efficiently and tightly to DNA and had specific affinity for sequences at the viral origin of replication, whereas the 16S form bound less efficiently to DNA and exhibited very little specificity for origin-containing DNA sequences. It is therefore likely that the active DNA-binding species of T antigen isolated from infected cells is the 5 to 7S form. (Author abstract) (43 Refs)

41. PRODUCTION OF A T-ANTIGEN-RELATED PROTEIN IN MAMMALIAN CELLS AFTER STABLE TRANSFORMATION WITH A CLONED SV40 GENE FRAGMENT.

Horst J, Jacob E, Weckler C, Deppert W
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Hoppe Seylers Z Physiol Chem; 363(4):445-448 1982

A recombinant plasmid based on pBR322 has been constructed which carries the replicator proximal early region of SV40 DNA, including the viral origin of replication (ORI). It lacks a major part of the tumor antigen 3'-coding region, the large T-antigen termination codon and the polyadenylation site. The recombinant plasmid was transferred together with the herpes simplex virus thymidine kinase gene, as a selectable marker into mouse LTK- cells. Integration and expression of the cloned SV40 gene fragment in TK+ transformants could be demonstrated by DNA restriction and blot hybridization and by immunofluorescence techniques. (Author abstract) (12 Refs)

TUMOR ASSOCIATED TRANSPLANTATION ANTIGENS

42. HETEROGENEITY OF TUMORIGENICITY PHENOTYPE IN MURINE TUMORS. CHARACTERIZATION OF TUMOR CLONES ISOLATED FROM PRIMARY 3-METHYLCHOLANTHRENE-INDUCED FIBROSARCOMAS.

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Transplantation; 33(4):387-392 1982

In this study we have characterized three series of clonal populations isolated from primary murine fibrosarcomas induced with three different doses of the chemical carcinogen, 3-methylcholanthrene (3-MCA). Clones were evaluated for their in vivo growth rates after transplantation into normal syngeneic animals, and for immunological cross-protection toward clones derived from the same tumor. A pattern of reactivity emerged from these studies which supports, at the single-cell level, existing theories regarding the correlation between the inducing dose of chemical carcinogen and the antigenicity of the resulting tumors. Clones from tumors induced with 10 mg of 3-MCA were found to be less tumorigenic than clones from tumors induced with 5 mg of 3-MCA. The 5-mg clones were in turn less tumorigenic than the 1-mg clones, all of which grew rapidly in normal animals. Related clones from each tumor were found for the most part to be immunologically noncross-reactive with other clones from the same tumor, suggesting that subpopulations of tumor cells expressing different tumor-specific transplantation antigens (TSTAs) may reside within single primary tumors. We have used these observations to formulate an hypothesis for the origin of antigenic heterogeneity in 3-MCA-induced tumors and as the basis for a discussion of the relationship between cell transformation and the appearance at the cell surface of tumor-specific transplantation antigens. (Author abstract) (19 Refs)

CLINICAL DIAGNOSTIC STUDIES

43. CYTOLOGIC DIAGNOSIS OF TRANSITIONAL CELL CARCINOMA BY IMMUNOCHEMICAL DETECTION OF TUMOR NUCLEOLAR ANTIGENS (MEETING ABSTRACT)

Scardino PT, Jurco S
No affiliation given
77th Annual Meeting of the American Urological Association, Inc May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Nucleoli isolated from HeLa S3 cells were used to produce a rabbit antiserum capable of binding nucleoli of transitional cell carcinomas (TCCa). Cross reactivity of the antiserum with normal nucleoli was markedly reduced by absorption with fetal bovine serum, pooled human serum, kidney acetone powder, and nucleolar preparations from normal human liver or placenta. This anti-nucleolar antiserum exhibits strong reactivity at dilutions of 1:400-1:1600 in immunofluorescence and immunoperoxidase assays performed on frozen sections of human bladder cancer, prostatic cancer and renal cell carcinoma. These assays can also be performed on fresh cytology specimens fixed in acetone or ethanol, although the immunoperoxidase technique requires prior quenching of endogenous red cell peroxidase to minimize nonspecific background staining. Voided urine specimens, bladder washings and renal pelvic washings were obtained from over 100 normal individuals and patients with TCCa. Specimens were placed on ice until centrifuged at 4C on the same day. The cellular pellet was resuspended in Hank's balanced salt solution and cytocentrifuged to prepare 6-18 slides for the assay. The slides were immediately fixed in cold acetone for 30 minutes and stored at room temperature. A standard indirect immunofluorescence or immunoperoxidase assay was performed, incorporating negative and positive controls with each group of slides. Bright nucleolar staining was consistently seen only in specimens from patients with TCCa. (no Refs)

44. EPSTEIN-BARR VIRUS-INDUCED DISEASES IN MALES WITH THE X-LINKED LYMPHOPROLIFERATIVE SYNDROME (MEETING ABSTRACT)

Purtilo DT, Harada S
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Lab Invest; 46(1):66A 1982

Analyses of 100 patients with the x-linked lymphoproliferative syndrome (XLP) in 25 kindreds revealed four major interrelated phenotypes: infectious mononucleosis (IM), malignant B cell lymphoma, aplastic anemia, and hypogammaglobulinemia. Eighty-one of the patients have died. Two males were asymptomatic but showed immunodeficiency to Epstein-Barr virus (EBV). Seventy-five patients had the IM phenotype and, concurrently, 17 patients of this group had aplastic anemia. All patients with aplastic anemia died within a week. Aplastic anemia did not accompany hypogammaglobulinemia or malignant lymphoma phenotypes. Hypogammaglobulinemia was detected before IM in three patients, followed IM in five cases, and was not associated with IM in 11 boys. Nine cases of IM appeared to have evolved into malignant lymphoma. However, the majority of patients with malignant lymphoma showed no obvious antecedent IM. One patient had IM following recurrent malignant lymphoma. Twenty-six of 35 lymphomas were in the terminal ileum. Results of immunologic and virologic studies of 15 survivors revealed combined variable immunodeficient responses to EBV-specific antigens. Patients with phenotypes of XLP should be investigated for immunodeficiency to EBV. Persons with inherited or acquired immunodeficiency may be vulnerable to life-threatening EBV-induced diseases. (no Refs)

45. ASYMPTOMATIC TYPE C VIRUS CARRIERS IN THE FAMILY OF AN ADULT T CELL LEUKEMIA PATIENT.

Miyoshi I, Taguchi H, Fujishita M, Niiya K, Kitagawa T, Ohtsuki Y, Akagi T
Dept. Medicine, Kochi Medical Sch., Oko-cho, Nankoku-shi, Kochi-ken 781-51, Japan
Gan; 73(2):339-340 1982

Serologic and virologic studies were performed in 14 members of the family of a 49-yr-old male patient with adult T cell leukemia (ATL). The patient and family lived in Kochi, an area where the incidence of ATL appears to be relatively high. ATL antigens (ATLA) and Type C virus particles were detected in short-term cultures of peripheral lymphocytes from 4/5 family members who were ATLA antibody positive. The five ATLA antibody positive family members were all asymptomatic and hematologically normal except for one member, in whom a persistent leukocytosis with several percent abnormal lymphocytes had been observed for two yr. It was not yet determined whether vertical or horizontal infection was involved in the virus transmission in this family. (5 Refs)

46. THE ASSOCIATION OF HAIRY CELL LEUKEMIA WITH UNUSUAL IMMUNOLOGIC DISORDERS.

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Dept. Internal Medicine, Univ. Iowa Hosp. and Clinics, Iowa City, IA, 52242
Arch Intern Med; 142(5):902-903 1982

Hairy cell leukemia is a rare disease, probably of B-lymphocyte origin, that has been reported to rarely occur with polyarteritis nodosa. The records of 31 patients with hairy cell leukemia were reviewed for an association with other disorders of the immune system; such an association was found more often than previously suspected. Four cases are discussed - one with hepatitis B surface antigen-positive polyarteritis nodosa and another with an IgA (kappa) monoclonal gammopathy and amyloidosis of the kidney, liver, and small bowel. The other two patients had cutaneous vasculitis, one of which was a rare form of leukocytoclastic angiitis - erythema elevatum diutinum. Because the number of patients in this study is small, it is impossible to say whether the association of hairy cell leukemia with any of these immunologic disorders adversely affects survival. (Author abstract) (13 Refs)

47. LEUKEMIA AND GLYCOLIPID AND GLYCOPROTEIN MARKERS.

Ishii Y, Kikuchi K
First Dept. Pathology, Sapporo Medical Univ., Sapporo, Japan
Nippon Rinsho; 39(8):2756-2767 1981

As glycoprotein (GP) markers, human lymphoid stem cell (LSC) contains common acute lymphocytic leukemia (ALL) antigen (mol wt 100,000), BA-2 antigen (mol wt 24,000), and Ia antigen. Ia antigen is made of two subunits: alpha-chain (mol wt 34,000) and beta-chain (mol wt 29,000) and also widely distributed in other hematopoietic cells. Glycolipid (GL) markers specific to LSC are not yet known. GP and GL markers specific to human pre-B cells are not yet clearly known. Antigen, OKT9 (mol wt 190,000) detected with monoclonal antibody is thought to be such a marker. Human pre-B cells contain GP such as cALL or BA-2 common to those of LSC. Also, B1 protein (mol wt 30,000) and FMC1 antigen are known as general B cell markers. Thymus cells located under the thymus cortex membrane has Thy-1, a GP, but which was not found in the thymus cortex cells, which have sialoglycoprotein (HTL antigen, mol wt 48,000). The presence of GL marker reflecting differentiation of thymus cells is unclear. Two GP antigens, Tgp72 (mol wt 72,000) and Leu-4 (mol wt 20,000) are known as general markers of human thymus T cells. Several other GP are also known. A pan B cell marker, B1, which differs from Ia or Ig is known. Some other markers were also found. Such markers appear or disappear in response to differentiation and maturity, and therefore, the source of leukemia can be known by checking for such markers. (65 Refs) (In JPN)

48. DETECTION OF A HUMAN MELANOMA-ASSOCIATED ANTIGEN, P97, IN HISTOLOGICAL SECTIONS OF PRIMARY HUMAN MELANOMAS.

Garrigues HJ, Tilgen W, Hellstrom I, Franke W, Hellstrom KE
Program in Tumor Immunology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
Int J Cancer; 29(5):511-515 1982

The unlabeled antibody technique of Sternberger was used to study the localization in histological sections of human melanoma-associated antigen p97, which is defined by a monoclonal antibody. The antigen was detected in 8 of 10 primary skin melanomas, in 6 of 7 metastatic melanomas and in 2 of 2 compound nevi. It was localized at the cell surface, the cytoplasm and the nucleus always being negative. The antigen was not seen in cells from three basal cell carcinomas, one squamous cell carcinoma, one leiomyosarcoma, or in samples of normal skin (including keratinocytes, connective tissue consisting of collagenous and elastic fibers, fibroblasts, sebaceous glands, blood vessels, smooth muscles, or inflammatory cells such as granulocytes, lymphocytes and macrophages), kidney or lung. There was, however, staining of some cells in the secretory segment of eccrine sweat glands from two patients, possibly corresponding to myoepithelial cells. Antigen expression was somewhat variable between cells from different melanomas as well as between individual cells from the same melanoma. The possible diagnostic value of this procedure for identification and classification of melanomas is discussed. (Author abstract) (24 Refs)

49. IMMUNOHISTOCHEMICAL ANALYSIS OF THE DISTRIBUTION OF LYMPHOCYTE SUBPOPULATIONS IN HODGKIN'S DISEASE.

Borowitz MJ, Croker BP, Metzgar RS
Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710
Cancer Treat Rep; 66(4):667-674 1982

We studied the histologic distribution of lymphocyte subpopulations in Hodgkin's disease. Involved tissues from 15 patients were stained by an indirect immunoperoxidase procedure for a variety of lymphocyte surface antigens using monoclonal antibodies. In most cases, there were more T cells than B cells, and Reed-Sternberg cells were found in T-cell-rich areas. Except in lymphocyte-depleted Hodgkin's disease, helper-T antigen-positive (TH) cells greatly outnumbered cytotoxic-suppressor antigen-positive cells. Moreover, TH cells showed a preferential association with Reed-Sternberg cells. Lymphocytes surrounding Reed-Sternberg cells often expressed the transferrin receptor, a marker of cell activation. Our results do not support the hypothesis that the lymphocytes in Hodgkin's disease represent a cytotoxic T-cell response to neoplastic cells, except perhaps in the lymphocyte-depleted subtype. (Author abstract) (24 Refs)

50. SCLEROSIS OF HILAR AND EXTRAHEPATIC BILE DUCTS: CRITERIA FOR DISTINCTION OF BENIGN AND MALIGNANT DISEASE (MEETING ABSTRACT)

Qualman SJ, Haupt HM, Bauer TW, Taxy JB
Department of Pathology, The Johns Hopkins Medical Institutions, Baltimore, MD
71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.

The distinction of hilar bile duct adenocarcinomas (Klatskin tumors) from benign sclerotic biliary lesions can be difficult histologically. Seven autopsy-proven cases of Klatskin tumors were compared with surgical material from 16 patients with sclerotic extrahepatic biliary lesions. Immunoperoxidase studies for tumor-associated antigens were performed on surgical cases only. In the autopsy cases, six tumors were localized to the hilum and liver; the average survival was 14 months following diagnosis. Histologically, this was a scirrhous glandular neoplasm with irregularly shaped lumina, obvious cytologic atypia (six of seven), and perineural invasion (seven of seven). Although all 16 surgical cases exhibited a similar scirrhous histologic pattern, only 10 were clinically thought to be tumors. Of these, eight exhibited either the atypia or perineural invasion observed in the autopsy cases; with one or both present on frozen section. Two of eight showed focal intracellular positivity for ferritin antigen not seen in clinically benign cases. Tumor location often precluded a definitive resection. Follow-up (4 to 19 months) revealed deaths in two of the eight patients with histologically confirmed tumors only. Our morphologic evaluation indicates that a diagnosis of Klatskin tumor can be established, even on frozen section, based on the frequency of severe cytologic atypia and perineural invasion. (no Refs)

51. PANCREATIC CARCINOMA ASSOCIATED ANTIGEN: A MARKER FOR PANCREATIC CARCINOMA (MEETING ABSTRACT)

Nadji M, Ganjei P, Shimano T, Chu TM, Morales AR
Department of Pathology, University of Miami, Miami, FL
Lab Invest; 46(1):60A 1982

Pancrease cancer-associated antigen (PCAA), a glycoprotein that has been shown to be elevated in patients with pancreatic carcinomas, was evaluated as a histologic marker for pancreatic carcinomas. Antibody to purified PCAA was raised in a rabbit and was treated with normal human serum and normal colon. The peroxidase-antiperoxidase stain was performed on paraffin sections of 47 pancreatic carcinomas and 12 non-neoplastic pancreatic lesions. Forty-nine benign and malignant nonpancreatic neoplasms were also included in this study. Positive reaction for PCAA was demonstrated in 45 of pancreatic carcinomas. None of the 12 non-neoplastic pancreatic lesions stained for PCAA. Of the nonpancreatic neoplasms, only 29 per cent of colonic and gastric carcinomas reacted positively. Two examples of islet cells tumors or pancreas did not stain for PCAA. Our study indicates that PCAA can be used as an immunohistologic marker for differentiating pancreatic carcinomas from histologically atypical nonmalignant lesions. Furthermore, a positive immunoperoxidase reaction for PCAA in a metastatic carcinoma of undetermined origin is strongly indicative of a primary tumor of the pancreas or gastrointestinal tract. (no Refs)

52. IDENTIFICATION OF BLADDER CANCER ASSOCIATED ANTIGENS BY TWO-DIMENSIONAL IMMUNOELECTROPHORESIS (MEETING ABSTRACT)

Hewitt CW, Shultz SM, Cote J, Miller B, Martin D
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association Missouri. American Urological Association 254 pp., 1982.

Urine specimens collected from bladder carcinoma patients and normal individuals were analyzed using two-dimensional immunoelectrophoresis (2D-IEP) in an effort to identify bladder tumor associated antigens. Only urine samples determined to be sterile by bacteriological culture were included in the study. Urine samples were concentrated 100 X by ultrafiltration using an Amicon PM-10 ultrafilter. Rabbit anti-bladder cancer urine sera was raised by multiple injections of a combined sample of a concentrated urine collected from 9 bladder carcinoma individuals for use in the 2D-IEP procedure. Preliminary results using polyacrylamide gel electrophoresis demonstrated that a combined sample of normal urine could be resolved into approximately 1 to 3 protein bands, but a single concentrated bladder cancer urine could be resolved into approximately 11 protein bands. However, 2D-IEP resolved this same concentrated bladder cancer urine into at least 17 antigen bands, thus demonstrating the sensitivity of the technique. Using 2D-IEP we found a significant difference in the number of slow migrating antigens after comparing normal and bladder cancer concentrated urines. Bladder cancer urines averaged 5.9 bands (9) in the slow migrating region, whereas normal urines averaged 3.0 bands (6). An advantage to the use of a 2D-IEP for urine analysis is that not only does this procedure separate unknown urine antigens very effectively, but it also provides information concerning the relative concentration of the antigen. (no Refs)

53. HUMAN BLADDER TUMOR ASSOCIATED SURFACE ANTIGENS (MEETING ABSTRACT)

Sramek SJ, Reichert DF, Smith KO, Lamm DL
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

A rabbit antiserum was prepared against the human transitional cell carcinoma cell line T24 to characterize possible tumor associated surface antigens. T24 antiserum demonstrated significant reactivity with human bladder tumor antigens and normal bladder antigens by radioimmunoassay (RIA). After repetitive absorption with a pool of antigens collected from normal urine sediments no reactivity with normal bladder antigens could be detected by RIA. The absorbed rabbit antiserum was tested with T24 labeled by one of two methods. Lactoperoxidase-catalyzed radioiodination of intact cells was used to label surface proteins and metabolic labeling with C14 glucosamine was used to label glycoproteins. The immune complexes were isolated on sepharose-bound staphylococcal protein A and then analyzed by SDS (sodium dodecyl sulfate) polyacrylamide gel electrophoresis. The majority of the I-125 radioactivity isolated by the immune serum was distributed in seven peaks with the following molecular weights: 1) 170K; 2) 130K; 3) 120K; 4) 70K; 5) 45K; 6) 42K; 7) less than 30 K. In metabolically-labeled cells, glucosamine radioactivity coincided with peaks 3, 6, and 7. The T24 extract released two proteins from patient immune complexes with a mobility in SDS gle identical to peaks 3 and 5. The rabbit anti-T24 serum appears to identify a family of surface and glycosylated tumor-associated antigens. Two of these antigens may be similar to circulating antigens in immune complexes from patients with transitional cell carcinoma. (no Refs)

54. THE USE OF AVIDIN-BIOTIN-PEROXIDASE COMPLEX (ABC) IMMUNOPEROXIDASE TECHNIQUE FOR IDENTIFICATION OF CELL SURFACE A, B, OR H BLOOD GROUP ANTIGENS IN BLADDER CARCINOMA: A COMPARISON BETWEEN ABC AND SPECIFIC RED CELL ADHERENCE (SRCA) TECHNIQUES (MEETING ABSTRACT)

Newman AJ, Carlton CE, Murphy WM
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

The major blood antigens A, B, or O (H) are present on normal urothelium. The presence or absence of these antigens on the cell surface of bladder tumors, as measured by the specific red cell adherence (SRCA) technique, has been shown to have prognostic value. In a series of 322 patients with superficial bladder tumors, we found that 71 of the 99 patients with a negative SRCA reaction subsequently developed an invasive lesion. While encouraging, this still left a 30 percent false negative rate. In an effort to increase the sensitivity of the assay, we have applied the avidin-biotin-peroxidase complex (ABC) immunoperoxidase technique of Hsu and coworkers to a series of 100 randomly selected formalin-fixed bladder tumor specimens from the prior SRCA study. One of us (WMM) did all of the ABC histochemical staining with no knowledge of the subsequent clinical course which consisted of either no recurrence in 5 years (25 cases), multiple superficial recurrences (25 cases), recurrence with invasion (25 cases); 25 cases represented transitional cell carcinoma with muscle invasion. Based upon recent data by Allen and coworkers showing that the purified Ulex europaeus lectin agglutinates erythrocytes of all three blood groups with little distinction between types O (H) and B, we have utilized biotinylated purified Ulex as the primary antisera in the ABC technique for all blood types. All of the invasive tumors showed delection of blood group antigen as previously found with the SRCA technique. The false negative rate using the ABC technique was only 10 percent (3 of 28). (no Refs)

55. MEASUREMENT OF HUMAN PROSTATE SPECIFIC ANTIGEN IN BENIGN AND MALIGNANT PROSTATIC TISSUE (MEETING ABSTRACT)

Stein BS, Peterson RO, Vangore SK, Kendall AR
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

The detection of human prostate specific antigen (PSA) in metastatic disease of unknown primary origin would help to properly identify the prostate as the source. The sensitivity and specificity of the tissue detection of PSA by immuno-peroxidase methods needs to be established first however. In order to determine the ability to detect PSA in prostatic tissue, we studied 52 patients with benign prostatic hyperplasia (BPH) and 30 patients with adenocarcinoma of the prostate. Routine 5 micron unstained sections of the prostatectomy specimen were examined for the presence of PSA using the Dako PAP (prostatic acid phosphatase) kit. All 52 patients with BPH demonstrated the presence of PSA in the acini. Major ducts, lined by transitional epithelium, were negative. Thirty patients with carcinoma were studied. Of these 24 (80%) demonstrated PSA in the tumor cells. The remaining 6 patients were all poorly differentiated tumors (Gleason grade 8-10). Thus, immuno-peroxidase determination of PSA appears to be reliable in well or moderately differentiated tumors, but is only helpful in poorly differentiated lesions when the antigen is isolated. (no Refs)

56. CELL SURFACE ANTIGENS IN THE BENIGN AND MALIGNANT PROSTATES (MEETING ABSTRACT)

McDermott DW, Lin CW, Chapman CM, Proppe KH, Prout GR
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Extensive studies have indicated that the loss of cell surface antigens (A, B, and H) in transitional cell carcinoma of the bladder correlated with subsequent development of invasive disease. However, few have reported studies on the cell surface antigens of the prostate. The objective of the present study is to evaluate these antigens in the benign and malignant prostate to see whether a similar correlation occurs. An immunoperoxidase method was used to stain the A, B, and H antigens in approximately ten cases each of normal prostate, benign prostatic hyperplasia (BPH) and well, moderately and poorly differentiated adenocarcinomas of the prostate. Positive controls in all stained sections were red blood cells and endothelial cells lining vessels. Negative controls were stromal cells, lymphocytes and leukocytes. In normal prostates obtained from males of age 18 to 37, variable glandular staining for the antigens was exhibited. In BPH, variable but more intense staining was present in hypertrophied glands. In carcinomas, there was a gradual loss of staining of acini from well to moderately and to poorly differentiated adenocarcinomas. Although the biological significance of these findings is not clear at the present time and may warrant further investigations, results from the study indicate that the staining would have very little prognostic significance in prostatic cancer due to the variable staining in both normal and BPH as well as in a significant number of carcinomas. (no Refs)

57. EVALUATION OF PROSTATIC SPECIFIC ACID PHOSPHATASE AND PROSTATIC SPECIFIC ANTIGEN IN IDENTIFICATION OF PROSTATIC CANCER (MEETING ABSTRACT)

Allhoff EP, Proppe KH, Chapman CM, Lin CW, Prout GR
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Undifferentiated carcinomas and metastases may pose difficult diagnostic problems. Both prostatic acid phosphatase antiserum (PSAP) and prostatic-specific antigen (PSA) have been reported to identify cells of prostatic origin. This study evaluated PSA and PSAP using an immunoperoxidase method. Neoplastic tissues from 21 patients were studied by conventional means and adjacent serial sections were stained for both PSAP and PSA. In 9 patients with prostatic, periprostatic and intravesical tumors, the cell type was in doubt. In 7 the neoplastic tissues stained positive (+) for PSAP. All 9 stained + for PSA, attesting to prostatic origin. Twelve metastases were studied because the sites of the primary tumor were unknown. Six stained + for PSAP. These and a 7th stained + for PSA. Histologically, the tissues from the prostate were concordant. Controls (40) of extraprostatic normal and neoplastic tissues stained negative for PSAP and PSA. A patient with prostatic carcinoma (CaP) underwent pelvic lymphadenectomy. One node was reported +; an involved supraclavicular node was removed later. All nodes were studied. The H and E (hemotoxylin and eosin) + pelvic node stained for PSAP and PSA; the supraclavicular node stained for PSA only. In 4/17 nodes, isolated or small clumps of cells stained for PSAP and PSA. Review of H and E preparations revealed tumor cells in the same sites. Further heterogeneity was demonstrated in 1 node with an area which stained for both markers and another which stained only for PSA. (no Refs)

58. DECREASED FALSE NEGATIVE CELL SURFACE ANTIGEN DETERMINATIONS IN UROTHELIUM OF O(H) PATIENTS USING AN IMMUNOPEROXIDASE TECHNIQUE (MEETING ABSTRACT)

Flanigan RC, King C, Primus J, Clark T, Sniecinski I, McRoberts JW
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

One factor hampering further progress in the use of cell surface antigen determinations of patients with urothelial malignancies has been the high incidence (approximately 40%) of false negative results in patients with blood group O(H) antigen using the standard red cell adherence (SRCA) test. This report details results from our laboratory using a new immunoperoxidase technique to evaluate antigenicity in normal ureters of patients with O(H) blood group. We have compared the reliability of this method with the SRCA test first described by Kovarik and Davidson and our 'bridge' modification of their technique. Multiple sections of 8 ureters were tested by each of the three methods described above. Seven of the 8 ureters were positive for cell surface antigen, one was consistently negative by all methods tested. Of the 7 specimens positive for cell surface antigen 65% (20/31) of the sections tested by SRCA were positive, 88% (36/41) tested by the 'bridge' modification of RCA were positive, and 96% (26/27) of the sections tested by imunoperoxidase were positive. (no Refs)

59. HEREDITARY ADENOMATOSIS OF THE COLON AND RECTUM: RELEVANCE TO CANCER PROMOTION AND CANCER CONTROL IN HUMANS.

Kopelovich L
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer Genet Cytogenet; 5(4):333-351 1982

Means of detecting persons at risk for colorectal cancers are described. SF cells, derived from normal-appearing biopsies of ACR gene carriers, appear to exist in an initiated state as the result of a dominant mutation. Topics discussed in relation to ACR and SF cells and colorectal neoplasms include the following: membrane-associated parameters, metabolic alterations, differential susceptiblity to transformation by chemical and physical agents and oncogenic viruses, cancer-related antigens, tissue culture studies, tumor promotion, genetic mechanisms, and cancer prognosis and control. (141 Refs)

OTHER RELATED STUDIES

60. QUANTITATIVE CYTOLOGY IN MYELOMA RESEARCH.

Barlogie B, Latreille J, Alexanian R, Swartzendruber DE, Smallwood L, Maddox AM, Raber MN, Drewinko B
Dept. Developemental Therapeutics, M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030
Clin Haematol; 11(1):19-46 1982

The role of quantitative cytology in myeloma research is discussed. Cytometric probes applicable to myeloma research include markers of neoplasia or tumor differentiation and cytokinetic descriptors. DNA content measurements may provide prognostically relevant information on intrinsic tumor cell properties such as ploidy and proliferative activity. Additional methods of characterizing the minor proportion of diploid plasma cells include analysis of RNA, overall protein, cytoplasmic Ig, and nucleolar antigen content. Cytokinetic marker techniques include DNA specific probes, DNA denaturation, and quenching of DNA probes. (58 Refs)

61. IMMUNOHISTOCHEMISTRY IN MODERN PATHOLOGY.

Ulich TP
No affiliation given
West J Med; 136(5):421-422 1982

Utility of immunohistochemistry in the pathology laboratory is discussed; the technique allows recognition of tissue antigens not identifiable by either routine light or electron microscopy. Immunofluorescence and immunoperoxidase staining allow the differential diagnosis of neoplasms (differentiation of lymphomas from nonlymphoid neoplasms, reactive lymphoid hyperplasia from lymphoma, primary pulmonary adenocarcinoma from metastatic prostatic carcinoma). Discovery of organ-specific antigens and the resulting availability of tumor specific antibodies, and the expanding technology of monoclonal antibody production, will increase the diagnostic value of immunohistochemistry. (2 Refs)

62. NATURAL ANTIBODIES TO CELL-SURFACE ANTIGENS OF HUMAN ASTROCYTOMA.

Pfreundschuh M, Rohrich M, Piotrowski W, Berlit P, Penzholz H
Med. Univ. Poliklinik Heidelberg, Univ. Heidelberg, Heidelberg, W. Germany
Int J Cancer; 29(5):517-521 1982

Sera of 200 non-transfused healthy male blood donors were tested for antibody reactivity to cell-surface antigens of cultured astrocytoma cells. Positive reactions were observed only rarely by protein-A assay (PA), in about half the cases by immune adherence assay (IA) and in nearly all cases by anti-C3 mixed hemadsorption assay (C3-MHA). In general, titers were low and only seven sera showed reactivity at 1:1,000. Serum 537 showed the strongest reaction. The anti-astrocytoma reactivity in this serum was due to an IgG antibody. Extensive absorption analysis with a panel of cell lines and fresh cells of both benign and malignant origin, as well as fetal cells, revealed that this serum detected an antigen that was present on most neural-crest-derived tumors (astrocytomas, melanomas and neuroblastomas), on very few other malignant tumors and on fetal brain. The antigen detected by serum 537 shows close relationship to the astrocytoma antigen AJ which had been defined by the serum of a patient with astrocytoma. Both antigens appear to be differentiation antigens present predominantly on non-epithelial neoplasms. The antigen detected by serum 537 is heat-stable and pronase-resistant. The sera of two other healthy donors apparently had a similar specificity, whereas the four other high-titered sera and all other sera detected Class-III antigens which were non-specific and not tumor-restricted. (Author abstract) (12 Refs)

63. EXPRESSION OF A MONOCLONAL ANTIBODY-DEFINED LIVER-ASSOCIATED ANTIGEN IN NORMAL RAT HEPATOCYTES AND HEPATOCELLULAR CARCINOMA CELLS.

Holmes CH, Gunn B, Austin EB, Embleton MJ, Baldwin RW
Cancer Res. Campaign Lab., Univ. Nottingham, University Park, Nottingham, NG7 2RD, England
Int J Cancer; 29(5):559-565 1982

In order to examine changes in the expression of normal cellular antigens during hepatocarcinogenesis, we have developed and characterized a monoclonal antibody detecting an antigen which is particularly associated with adult rat hepatocytes. The antibody showed no reactivity with a range of freshly-prepared normal syngeneic adult rat cell types, but showed strong reactivity with hepatocytes derived from several rat strains in antibody binding tests. Immunoperoxidase staining of sections of normal rat liver showed that the antigen was distributed throughout hepatocytes within the liver, but did not stain cells other than hepatocytes. The antigen detected by this monoclonal antibody was not detectable on a number of transplanted and primary dimethylaminoazobenzene-induced hepatomas. Preliminary data indicated that this monoclonal antibody may be suitable for use in flow cytofluorimetric sorting of mixed populations of normal and tumor cells, allowing the investigation of cell phenotypes during hepatocarcinogenesis. (Author abstract) (18 Refs)

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IMMUNOBIOLOGY AND CANCER
Tumor-Associated Antigens

SERIES CB05 No. 82/11 NOVEMBER, 1982

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DETECTION/ CHARACTERIZATION/ ISOLATION

1. EXPRESSION OF DR ANTIGENS IN FRESHLY FROZEN HUMAN TUMORS.

Thompson JJ, Herlyn MF, Elder DE, Clark WH, Steplewski Z, Koprowski H

Div. Surgical Pathology, Hosp. Univ. Pennsylvania, Box 527, 3400 Spruce St., Philadelphia, PA, 19104

Hybridoma; 1(2):161-168 1982

Using frozen tissue sections, a monoclonal antibody (WI 691-13-17) known to detect an epitope common to all DR antigens on the beta (light) chain of DR antigens, and a two-step indirect immunoperoxidase technique, DR antigens were found on all metastatic lesions tested and on many primary tumors and their histogenetic precursors. In all, 106 benign and malignant tumors and 255 normal tissues were tested. All metastatic and most of the primary tumors apparently expressed DR antigens; malignancies derived from ectodermal, endodermal, and mesodermal embryonic layers all showed DR expression. DR antigen expression was seen in all lesions of the melanocytic neoplastic system as defined by Elder and co-workers, with pre-

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cursor lesions demonstrating relatively few positive cells, primary and metastatic lesions progressively more. A subpopulation of lymphocytes, macrophages, endothelial cells, and Langerhans cells also exhibited DR antigen expression. The quantitative intensity of staining among the cells of the lesions tested ranged from negative to variable amounts. This technique allows individual cells to be assessed for antigen expression and presumably more accurately reflects in vivo antigen expression than results obtained from cells selected by tissue culture methods. (13 Refs)

2. DETECTION OF A TUMOR-ASSOCIATED ANTIGEN ON THE SURFACE OF HUMAN MYELOGENOUS LEUKEMIA CELLS.

Malcolm AJ, Shipman RC, Levy JG

Dept. Microbiology, Univ. British Columbia, Vancouver, British Columbia V6T 1W5, Canada

J Immunol; 128(6):2599-2603 1982

Membrane extracts of human acute myelogenous leukemia cells were passed over immunoadsorbent columns containing antibodies directed to equivalent preparations of pooled normal peripheral blood leukocytes. This material, when compared to equivalent normal cell preparations on nonreducing polyacrylamide gels, demonstrated the presence of four unique bands, not found in normal cell preparations. With the use of a previously described leukemia-specific heteroantiserum, these bands, after elution, were tested for reactivity with the antiserum. The eluted material containing reactive antigen was used to immunize rabbits. The resulting antiserum showed strong reactivity with myelogenous leukemic cell extracts and none with normal materials. A series of bone marrow samples from patients with a variety of lymphoproliferative and myeloproliferative disorders were tested with this antiserum in the fluorescence-activated cell sorter. In every instance, bone marrow cells from patients with acute myelogenous leukemia and chronic myelogenous leukemia showed strong positive fluorescence with this antiserum. However, no bone marrow cells from patients with lymphoproliferative disorders or patients with other leukemias showed any fluorescence above background with this antiserum. (Author abstract) (17 Refs)

3. A HUMAN THY-1-LIKE ANTIGEN EXPRESSED ON CULTURED LEUKEMIC T-CELLS.

Saji F, Tanigaki N

(c/o Tanigaki) Dept. Molecular Immunology, Roswell Park Memorial Inst., Buffalo, NY, 14263

Immunogenetics; 15(6):551-563 1982

A human cell membrane antigen that is highly T-cell specific among a number of leukocyte cell lines was isolated from cells of a human T-cell leukemia cell line, SKW-3. In addition to the high specificity to T-cell-type cell lines, the isolated antigen showed the following characteristics: (1) It is an acidic glycoprotein of approximately 30,000 daltons that has a charge heterogeneity and probably a disulfide bond(s); (2) Its antigenicity is stable when treated with heat, acid, and various protein denaturants; (3) It is widely distributed in lymphoid and nonlymphoid tissues but is most predominant in brain. These features are similar, if not identical, to those reported for the Thy-1 antigen of mouse or rat and have raised the possibility that this cell membrane antigen may correspond to human 'lymphocyte' Thy-1 antigen, the counterpart of human 'brain' Thy-1 antigen. (Author abstract) (28 Refs)

4. VIL-A1, A MONOCLONAL ANTIBODY REACTIVE WITH COMMON ACUTE LYMPHATIC LEUKEMIA CELLS.

Knapp W, Majdic O, Bettelheim P, Liszka K

Inst. Immunology, Borschkegasse 8A, A-1090 Vienna, Austria

Leuk Res; 6(2):137-147 1982

Generation and characterization of a monoclonal antibody (VIL-A1) raised against Reh cells which specifically reacts with the common acute lymphoblastic leukemia associated (CALL) antigen are described. Immunoelectrophoresis of VIL-A1 showed that the antibody is of the IgM kappa type. Several established human cell lines were tested for their reactivity with VIL-A1 and the reactivity patterns are presented. The reactivity of VIL-A1 with leukemic cells from 97 patients were tested by immunofluorescence. Positive reactions were observed in non-B, non-T acute lymphatic leukemias and in terminal deoxynucleotidyl transferase (TdT) positive chronic myeloid leukemia blast crisis. The reactivity pattern of VIL-A1 and J5 was absolutely identical. VIL-A1 reacted with a membrane component of Reh-6 cells with a mol wt of approx 95,000 daltons. No VIL-A1 reactive component was detected in Raji cells. Not all VIL-A1 antigen bound to lecithin and the binding capacity was heterogenous. Unlabeled VIL-A1 antibody very efficiently blocked the binding of peroxidase-labeled VIL-A1 antibody to a CALL membrane preparation coated on polystyrene tubes. Preincubation with J5 antibody under capping conditions restricted the binding of VIL-A1 antibody, although incubated under non-capping conditions, to one pole of the cell and preincubation with VIL-A1 antibody under capping conditions restricted the binding of J5 antibody to one pole of the cell. Preincubation with negative control antibody had no such effect and left the normal diffuse and ring-staining pattern of both antibodies unchanged. Results showed that the VIL-A1 monoclonal antibody raised against Reh cells reacts with CALL cells but not with normal or malignant B or T lymphocytes. (34 Refs)

5. A MONOCLONAL ANTIBODY WITH ANTI-BURKITT LYMPHOMA SPECIFICITY. I. ANALYSIS OF HUMAN HAEMATOPOIETIC AND LYMPHOID CELL LINES.

Wiels J, Lenoir GM, Fellous M, Lipinski M, Salomon JC, Tetaud C, Tursz T

Laboratoire d'Immunologie Clinique, Institut G. Roussy, Rue C. Desmoulins, 94800 Villejuif, France

Int J Cancer; 29(6):653-658 1982

There is a hybridoma-produced monoclonal rat IgM (38-13) which appears to define a Burkitt's lymphoma-associated antigen (BLA). In this paper, we describe the reactivity of 38-13 with a panel of human hematopoietic and lymphoid cell lines. In indirect immunofluorescence (IF) assays, 15 of 26 Burkitt's lymphoma (BL) lines studied were clearly stained with 38-13 (from 13 to 100% positive cells) by microscope, with varying numbers of heavily labeled cells. In these positive cell lines, fluorescence-activated cell-sorter (FACS) analysis demonstrated that BLA was actually present on all the cells. Positive BL included Epstein-Barr virus (EBV) genome-carrying lines and EBV-negative ones; thus, BLA is not related to the presence of EBV. Most of the 15 BL cells that reacted with 38-13 contained a typical t(8;14) translocation, but had variant translocations such as t(2;8) and t(8;22). The cells were derived from BL patients of different geographical origins and clinical features. Four BL lines were poorly stained and seven were negative with 38-13 in IF assays. The 32 EBV-positive lymphoblastoid cell-lines (LCL) studied were negative. In three line pairs, consisting of a tumor line and an LCL from the same patient,

only the BL line was demonstrated to react with 38-13. A series of non-BL cells, including hematopoietic, lymphoid and solid tumor lines, all failed to react with 38-13. Various attempts to modulate the expression of BLA on BL cells were unsuccessful. However, it cannot be ruled out that BLA is actually a transient B-cell differentiation marker. (Author abstract) (18 Refs)

6. A NEW ACUTE LEUKEMIA-ASSOCIATED BLAST CELL ANTIGEN DETECTED BY A MONOCLONAL ANTIBODY.

Billing R, Lucero K, Shi BJ, Terasaki PI
Tissue Typing Lab., Dept. Surgery, Univ. California Los Angeles, 1000 Veteran Ave., Room 15-22, Los Angeles, CA, 90024
Blood; 59(6):1203-1206 1982

A monoclonal mouse antibody has been raised to the common acute lymphoblastic leukemia (cALL) cell line Reh. It is a cytotoxic antibody of the IgG2a subclass that reacts with leukemia cells from the following patients: 69% non-B non-T ALL, 50% T-ALL, 18% acute myeloblastic leukemia (AML), and 66% chronic myeloid leukemia (CML) blast crisis lymphoid cells. Other types of leukemia and all normal blood cells tested were negative, including T and B lymphocytes, granulocytes, monocytes, erythrocytes, and spleen cells. The detected antigen appears to be a type of blast cell antigen because it is also present on phytohemagglutinin (PHA) blast cells, myeloblast from normal bone marrow cells (by CFU-C), and all lymphoblastoid cell lines tested. Only one active antibody species could be detected by preparative isoelectric focusing on polyacrylamide gels and by protein-A-Sepharose affinity chromatography. (Author abstract) (17 Refs)

7. MOUSE MONOCLONAL ANTIBODY TO A MELANOMA-CARCINOMA-ASSOCIATED ANTIGEN SYNTHESIZED BY A HUMAN MELANOMA CELL LINE PROPAGATED IN SERUM-FREE MEDIUM.

Chee DO, Yonemoto RH, Leong SP, Richards GF, Smith VR, Klotz JL, Goto RM, Gascon RL, Drushella MM
Oncology Lab., Inc., Fiskeville, RI, 02823
Cancer Res; 42(8):3142-3147 1982

A monoclonal antibody, F11, was produced against a tumor-associated antigen from the spent medium of the M14 human malignant melanoma cell line which was grown continuously in serum-free medium. Ouchterlony double-diffusion study revealed that the F11 monoclonal antibody is an immunoglobulin G1. The F11 monoclonal antibody reacted positively with seven of eight (88%) melanoma, five of five (100%) carcinoma, zero of five normal, and zero of two lymphoblastoid cell lines by indirect immunofluorescence test. Also, by indirect immunofluorescence test, F11 monoclonal antibody reacted with cryostat sections from four of five (80%) melanomas, six of seven (86%) carcinomas, zero of one benign nevus, and zero of two benign breast diseases. By the indirect avidin:biotin:peroxidase complex immunoperoxidase method, the F11 monoclonal antibody reacted positively with cryostat sections from five of five (100%) melanomas, five of five (100%) breast cancers, two of two (100%) colon cancers, zero of one benign nevus, and zero of one Hodgkin's disease spleen. Thus, the tumor-associated antigen that the F11 monoclonal antibody recognizes appears to be expressed by melanomas and carcinomas, hence the designation melanoma-carcinoma-associated antigen. Microscopic observations disclosed that the melanoma-carcinoma-associated antigen is present in the cytoplasm, on the membrane of melanoma and carcinoma cells, and in the lumen of glandular structures of breast and colon carcinomas. The mol wt of the melanoma-carcinoma-associated antigen in spent medium from the M14 CEM cell line is 100,000 as determined by sodium dodecyl sulfate: polyacrylamide gel electrophoretic analysis of indirect immunoprecipitates obtained with the F11 monoclonal antibody. (Author abstract) (37 Refs)

8. USE OF MONOCLONAL ANTIBODIES IN DETECTION OF MELANOMA-ASSOCIATED ANTIGENS IN INTACT HUMAN TUMORS.

Thompson JJ, Herlyn MF, Clark WH, Elder DE, Steplewski Z, Koprowski H
Box 527 Surgical Pathology, Hosp. Univ. Pennsylvania, 3400 Spruce St., Philadelphia, PA, 19104
Am J Pathol; 107(3):357-361 1982

The use of antimelanoma monoclonal antibodies on tissue sections using a two-step indirect immunoperoxidase technique is reported. Antibodies 691-13-17 and 691-15-Nu4B reacted with dysplastic nevus cells and all melanomas tested, but not with normal skin melanocytes, intradermal nevi, or lentigines. Antibody 691-13-17, directed against DR antigen, reacted also with Langerhan's cells, macrophages, and a subpopulation of lymphocytes. Antibody 691-15-Nu4B reacted only with melanomas. The technique allows analysis of the expression of antigens by tumor cells in situ. (Author abstract) (11 Refs)

9. A, B, H ANTIGEN DETECTABILITY IN NORMAL AND NEOPLASTIC UROTHELIUM. INFLUENCE OF METHODOLOGIC FACTORS.

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Cancer; 49(12):2476-2484 1982

Markedly reduced or absent reactivity for the normally expressed A B H antigens in transitional cell carcinomas (TCCs) of the human urinary bladder appears to correlate with an aggressive clinical course. To evaluate the clinical applicability of this observation, the authors investigated the influence of methodologic variants as well as certain patient characteristics on urothelial A, B, H reactivity. Biopsy-obtained TCCs and/or normal mucosae from 104 patients were examined for the effect of fixation, paraffinization, and alcohol treatment. Variability due to the secretor status and blood group of the patient was evaluated in conjunction with methodologic factors. In the fresh-frozen state, the expected antigen was always detectable in normal mucosas but only in 69% of TCCs regardless of patient's secretor status and blood group (BG). Few normal mucosae (12%) but a large number of TCCs (46%) converted to negative after paraffin processing. Similar reduction in A, B, H reactivity was also noted when the tissues were treated with concentrations of alcohol comparable to those used in the paraffin procedure. Tumor antigens were more sensitive to alcohol. This suggested that in neoplastic cells ABH determinants are not only fewer but also disproportionately represented on polar (alcohol-soluble) molecules. Alcohol more profoundly affected tissues from nonsecretors probably because the proportion of alcohol-soluble A, B, H substances differs in secretors and nonsecretors. In the fresh-frozen state, the H antigen was detectable with the Ulex Europeus lectin in the majority of TCCs from BGO patients (79%) as well as in most tumors from BGA or B patients (90%) even in the absence of the expected A or B antigen. Alcohol treatment, however, more potently reduced reactivity for H rather than the other antigens, a phenomenon that also points to the significance of glycolipid extraction and explains the marked differences in the detectability of this antigen between fresh-frozen and paraffin-processed TCCs. (Author abstract) (24 Refs)

10. IMMUNOLOGICAL SPECIFICITY OF NOVIKOFF HEPATOMA CHROMATIN: ISOLATION OF THREE ANTIGENIC PROTEINS.

Stryjecka-Zimmer M, Schmidt WN, Briggs RC, Hnilica LS
Dept. Physiological Chemistry, Medical Sch., Lubartowska 85, 20-123 Lublin, Poland
Int J Biochem; 14(7):591-600 1982

Rabbits immunized with dehistonized Novikoff hepatoma (NH) or normal rat liver (NRL) elicited specific antibodies. Fractionation of nonhistone proteins from the NH group yielded three proteins (approx mol wt 39,000, 49,000 and 56,000) identified with the hepatoma antigenic complexes which showed significant reactivity with PAS staining, suggesting they were glycosylated. Three similar proteins from NRL were PAS negative, and did not react immunologically with antiserum to dehistonized NH chromatin. (49 Refs)

11. A NEW GLYCOPROTEIN ANTIGEN COMMON TO TERATOCARCINOMA, VISCERAL ENDODERM, AND RENAL TUBULAR BRUSH BORDER.

Ozawa M, Yonezawa S, Sato E, Muramatsu T
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Dev Biol; 91(2):351-359 1982

Glycoproteins were purified from teratocarcinoma OTT6050 by affinity chromatography on Dolichos biflorus agglutinin-agarose. The rabbit antiserum raised against the glycoproteins defined a new antigenic marker after absorption with sheep erythrocytes and particulate fraction of the mouse liver. The antigen was detected on the visceral endoderm of 7-day-old embryos, on the tubular brush border of the kidney in adult mice and on certain endodermal cells of teratocarcinomas. Upon sodium dodecyl sulfate-gel electrophoresis, the antigens from teratocarcinoma OTT6050 and from the kidney migrated as band(s) of mol wt around 500,000. Although the antigens from the two sources were immunologically identical, they should be different in carbohydrate sequence as judged from their behavior upon affinity chromatography on lectin-agarose. (Author abstract) (29 Refs)

12. A NEW MURINE CELL SURFACE DIFFERENTIATION ANTIGEN (LEUGP90) DEFINED BY A RAT MONOCLONAL ANTIBODY: CELLULAR DISTRIBUTION AND BIOCHEMICAL CHARACTERIZATION.

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J Immunol; 128(6):2664-2669 1982

Monoclonal antibodies to murine lymphocyte differentiation antigens were generated by fusing the mouse myeloma cell line X63-Ag8.653 with spleen cells derived from Lewis rats hyperimmunized with lymphoid cells from nude (C57BL/6) mice. One of these antibodies - designated 3MB1-recognizes a previously undescribed cell surface antigen. This antigen is expressed on 62% of spleen cells, 9% of thymus cells, and 98% of peritoneal macrophages. Virtually all LPS- and Con A-induced lymphoblasts carry this newly found antigen. The 3MB1 determinant is limited in its expression to leukocytes. It is not found in other tissues such as brain, liver, kidney, or on erythrocytes. Biochemical analysis reveals that the 3MB1 target antigen consists of a single chain glycoprotein with an approx mw of 90,000. (Author abstract) (43 Refs)

IMMUNOLOGICAL STUDIES

13. THE EFFECT OF TARGET CELL DIFFERENTIATION ON HUMAN NATURAL KILLER CELL ACTIVITY: A SPECIFIC DEFECT IN TARGET CELL BINDING AND EARLY ACTIVATION EVENTS.

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J Immunol; 129(1):413-418 1982

Induced differentiation of K562 and HL-60 cultures was associated with a concomitant decrease in natural killer (NK) susceptibility of these target cells. The erythroleukemic cell line K562 was induced to undergo erythroid differentiation with optimal concentrations of sodium butyrate or hemin, and HL-60, a promyelocytic leukemia cell line, was induced to differentiate along the myeloid series with dimethyl sulfoxide or along the monocytic lineage with 12-tetra-decanoylphorbol-13-acetate. The kinetics of cellular differentiation was closely associated with changes in susceptibility to NK-mediated lysis. Control experiments performed in the presence and absence of inducers and experiments with noninducible target cells suggest that the differentiation-related decrease in NK-mediated sensitivity is due to the nature of the induced target cells and not the agents per se. The differentiation-induced reduction in target cell susceptibility appeared to be largely specific for NK activity, since other mechanisms of cytolysis such as antibody-dependent cellular cytotoxicity, anomalous killing, and monocyte-mediated lysis were not changed compared to the untreated target cells. No differences were found in lectin-induced cytolysis of untreated and differentiated HL-60 cultures, although butyrate-induced K562 cells were less sensitive to this form of cytolysis. Pretreatment of NK cells with interferon resulted in elevated levels of lysis of both untreated and differentiated target cells but did not restore the susceptibility of the differentiated NK resistant (NKR) target cells to that of the untreated parent cell lines. The predominant reason for the lowered NK susceptibility of the induced target cells was a decrease in the NK binding ability of these cells. The NKR-differentiated K562 cultures were defective in inducing superoxide radical generation from Percoll-enriched NK cells. This induction is associated with an early post-recognition event in the NK lytic pathway. Further analysis of the surface molecules lost or gained during controlled differentiation may lead to a better understanding of NK-target antigens. (32 Refs)

14. TUMOR CELL DIFFERENTIATION MODULATES SUSCEPTIBILITY TO NATURAL KILLER CELLS.

Werkmeister J, Helfand SL, Haliotis T, Rubin P, Pross H, Roder J
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Cell Immunol; 69(1):122-127 1982

Induced differentiation in three human cell lines altered their sensitivity specifically to human natural killer (NK) cells by affecting their expression of NK target antigens. Differentiation of HL-60, a promyelocytic leukemia cell line, and the erythroleukemic cell line K562 was accompanied by a concomitant decrease in susceptibility to NK-mediated lysis whereas induction of MeWo melanoma cells resulted in an enhanced sensitivity to lysis. Our findings suggest that target cell susceptibility to NK-mediated lysis may in part be dependent on the stage of differentiation of the tumor cell target. (Author abstract) (23 Refs)

15. THYMIC ORIGIN OF THE PROLACTIN-DEPENDENT NB2 LYMPHOMA CELL LINE.

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Cancer Res; 42(8):3138-3141 1982

Blast cells in acute leukemia and lymphoma appear to be 'frozen' at various stages of lymphoid cell differentiation. The enzymatic and antigenic phenotypes expressed by these cells often correspond to the gene products of their normal precursors. We have used various immunocytochemical and enzymatic techniques to identify membrane, nuclear, and cytoplasmic markers associated with prolactin-dependent Nb2 lymphoma cell line. The Nb2 cells, whether stationary or in log-phase growth, did not express any surface immunoglobulin. However, 100% of the Nb2 cells bound both a monoclonal antibody raised to rat thymocyte W3/25-HLK, which specifically binds an antigenic determinant on rat T-helper cells, and second monoclonal antibody OX8-HL, which identifies rat nonhelper T-cells. Transmission electron microscopy showed no evidence of phagocytic vacuoles, and activity of the lysosomal enzyme muramidase was also absent. There was no evidence of the DNA polymerase enzyme terminal deoxynucleotidyl transferase. Alpha-Naphthyl acetate esterase activity was indicated in about 50% of the Nb2 cells by a faint particulate cytoplasmic staining similar to that found in thymocytes. Rosette formation with guinea pig erythrocytes, a property of mature rat thymocytes, was not observed with Nb2 cells. The data suggest that the Nb2 tumor may have arisen from a thymocyte at an intermediate stage of differentiation. The presence of Thy-like alpha-naphthyl acetate esterase pattern and the binding of both W3/25-HLK and OX8-HL support the thymic origin and relative immaturity of these lymphoid cells. It is becoming increasingly apparent that a significant proportion of lymphomas and leukemias also originate in undifferentiated thymic cells. (Author abstract) (15 Refs)

16. A MONOCLONAL ANTIBODY (MMA) THAT IDENTIFIES A DIFFERENTIATION ANTIGEN ON HUMAN MYELOMONOCYTIC CELLS.

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Clin Immunol Immunopathol; 23(2):172-188 1982

A monoclonal IgMkappa antibody (MMA) was produced against the human histocytic cell line, U-937. This antibody reacted by indirect immunofluorescence and complement-mediated lysis with adherent mononuclear cells and granulocytes. MMA was unreactive with circulating T and B cells, erythrocytes, and platelets. Depletion of MMA+ cells from blood mononuclear cell populations significantly reduced the reactivity of these cells to antigens and mitogens. The lymphoproliferative responses were restored by addition of 10% MMA+ cells. MMA is expressed by some T-cell lines (HSB-2, MOLT-3, MOLT-4) and mitogen-activated T cells, but not by B-cell lines or activated B cells. Studies using double immunofluorescence showed that 80% of activated T4+ and 10% of T8+ cells expressed MMA. The antigen is present on precursors of in vitro granulopoietic colony-forming cells. Malignant cells from patients with both acute and chronic myeloid leukemias express this antigen. The MMA antibody thus defines a unique differentiation antigen present on human myeloid cells, their precursors, and a subpopulation of activated T cells. (Author abstract) (45 Refs)

17. DETECTION OF TUMOR ANTIGENS BY SYNGENEIC ANTISERUM ON IN VITRO-TRANSFORMED TRACHEAL EPITHELIAL CELL LINE 2-10-1.

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Int J Cancer; 29(6):677-681 1982

Sera obtained from rats showing transplantation immunity to syngeneic, malignant epithelial cell line, 2-10-1, were used to identify antigens associated with transformation in vitro. The 2-10-1 cell line was derived from exposure of tracheal explants, in vitro, to the carcinogen N-methyl-N'-nitro-N-nitrosoguanidine (MNNG). Tumorigenic passages of the cell line were shown to have common antigenic determinants, shared by independently transformed malignant tracheal epithelial cell lines, as well as antigenic determinants that appear to be limited to the immunizing cell line, 2-10-1. Care was taken to ensure that antibodies were not produced against viral antigens or non-specifically absorbed serum components. Early passages of the 2-10-1 cell line were not tumorigenic in athymic BALB/c (nu/nu) mice, but became malignant with serial passage in vitro. Antigenic specificities recognized by 2-10-1 immune sera were also present on early-passage 2-10-1 cells that had not as yet acquired the malignant phenotype. Such antigen expression must be an early event in neoplastic development. (Author abstract) (20 Refs)

18. MONOCLONAL ANTIBODIES TO HUMAN LUNG TUMOR ANTIGENS DEMONSTRATED BY IMMUNOFLUORESCENCE AND IMMUNOPRECIPITATION.

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Cancer Res; 42(8):3187-3192 1982

Various studies have demonstrated the usefulness of monoclonal antibodies in recognizing discrete tumor antigenic determinants. The present study describes the tissue reactivity of monoclonal antibodies prepared against a squamous cell carcinoma of the lung. Antigens were purified from the tumor extract by anti-beta2 microglobulin affinity chromatography. These beta2-associated antigens demonstrated tumor specificity by the leukocyte adherence inhibition assay. Antibody-secreting hybridomas were generated by fusion of mouse myeloma cells with mouse spleen cells immunized with purified tumor antigens. Hybridomas were selected by a solid-phase tumor membrane-binding immunoassay. The target specificity of the secreted monoclonal antibodies was ascertained by radioimmunoprecipitation analysis and indirect immunofluorescence on various human tumor and normal tissue sections. Monoclonal antibody-secreting hybridomas 48.4.8 and 48.4.2 secreted immunoglobulin that selectively immunoprecipitated polypeptide fragments from human lung tumor membrane antigens. Hybridoma 9.2.2 secreted antibody that was strongly positive by indirect immunofluorescence on all tested lung squamous cell carcinomas. Adjacent or intervening normal lung tissue did not display significant immunofluorescence. Adenocarcinomas of the lung were negative or focally positive when focal squamous cell differentiation was present. Oat cell carcinomas were negative. The secreted antibody did not significantly stain three extrapulmonary tumors or a variety of normal tissues. (Author abstract) (21 Refs)

19. ANTIGENIC DIFFERENCES BETWEEN A PRIMARY HAMSTER LYMPHOSARCOMA AND ITS LIVER METASTASES.

Sherbet GV, Lakshmi MS, Risely GP, Shah SA, Tindle ME
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Experientia; 38(5):610-611 1982

An antiserum was raised in rabbits against a primary metastasizing lymphosarcoma (ML) of the hamster. This was made tumor-specific by absorption with normal hamster tissue extracts. Immunoglobulin-G was prepared and tested for its cytotoxicity towards cells derived from the primary tumor and its liver metastases. The ML-specific IgG was found to be 2-5x more cytotoxic for cells derived from the primary tumor compared to cells obtained from liver metastases. (Author abstract) (16 Refs)

20. ANTITUMOR IMMUNOLOGIC REACTIVITY IN THE RELATIVELY EARLY PERIOD AFTER CRYOSURGERY: EXPERIMENTAL STUDIES IN THE RAT.

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Second Dept. Surgery, Gifu Univ. Sch. Medicine, Gifu City, Japan
Cryobiology; 19(3):263-272 1982

An experimental investigation was performed on antitumor immunity in the relatively early postoperative period after cryosurgery, using a metastasizing rat's mammary tumor, MRMT-1. Two wk after its inoculation, surgical excision of the tumor, cryosurgery, surgical excision plus inoculation with freezing-thawing produced vaccine, or surgical excision plus fasting for 72 hr was performed, and postoperative follow-up was done on incidences of metastases, those of metastatic death, etc. Specific immunologic reactivity was examined in the surgical excision (SE) and cryosurgery (CR) groups. The FTV and fasting groups showed more metastatic deaths as compared with the SE group. The CR and SE groups did not differ significantly form each other in incidences of lung and lymph node metastases. Specific footpad reactivity at 2 and 3 wk after treatment was lower in the CR group than in the SE group. Winn's neutralization assay showed an inhibition of tumor growth at 1 and 3 wk after treatment both in the SE and in the CR groups, the inhibitory effect tending to be lower in the latter. Inactivated serum obtained at 1 wk after treatment showed a facilitation of tumor growth in the SE group and a tendency of tumor suppression in the CR group, showing a significant difference between them. A mild reduction in antitumor immunity seen in the relatively early postoperative period following cryosurgery probably was not due to a blocking effect by superfluous antigens. Rather it was considered to be due to activation of suppressor cells, consequent on cryosurgical stress, and/or slow and steady absorption of antigens. (Author abstract) (24 Refs)

21. A CLONED CELL LINE, MK1, POSSESSING IA ANTIGENS AND ACCESSORY CELL ACTIVITY.

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J Immunol; 128(6):2586-2594 1982

A new cell line, termed Mk1, was established by subcloning from M1+ cells derived from murine myeloid leukemia cell line cells, M1-, by coculture with conditioned medium containing a differentiation factor harvested from secondary cultures of embryonic fibroblasts. Mk1 cells, consisting of five clones (A to E), are dish-adherent cells with a few long processes and are nonspecific esterase-positive. These cell line cells have been maintained in the absence of conditioned medium. The capacity to ingest latex particles is low in Mk1 cells, but is significantly higher in both M1+ and Mm1 cells, the latter of which is a clonal subline of M1-cells. Fc receptors for IgG are always observed on 60 to 70% of each Mk1 cell clone, as well as on M1+ and Mm1 cells. Nevertheless, the phagocytic activity for EA (IgG antibody-sensitized sheep erythrocytes) is remarkably low in Mk1 and M1+ cells in comparison to Mm1 cells. Another marked difference between Mk1 and Mm1 cells is the expression of Ia antigen; Ia antigens detected by anti-Iaq and anti-Iak are found in the former, but not in the latter. The expression of Ia antigen in MK1 cells is dependent on the cell cycle, and is accompanied by the appearance of accessory cell activities for lymphocytes in primary and secondary anti-SRBC PFC responses as well as with the production of monokines that substitute for A cells in secondary anti-SRBC PFC responses and augment Con A responses of syngeneic thymocytes. Despite the expression of Ia antigens, Mk1 cells lack the ability to stimulate allogeneic lymphocytes in MLR, suggesting that either Ia on MK1 cells is different than that on other effective stimulator cells or that Mk1 cells lack additional features that contribute to MLR stimulation. Thus, Mk1 and Mm1 cells seem to be counterparts in the macrophage lineage; Mk1 cells as a model of A cells that are poorly phagocytic and Ia antigen-positive, and Mm1 cells as a model of scavengers that are highly phagocytic and lack A cell activity. (57 Refs)

22. IMMUNOGENIC VARIANTS OBTAINED BY MUTAGENESIS OF MOUSE MASTOCYTOMA P815: III. CLONAL ANALYSIS OF THE SYNGENEIC CYTOLYTIC T LYMPHOCYTE RESPONSE.

Maryanski JL, Van Snick J, Cerottini JC, Boon T
Ludwig Inst. Cancer Res., UCL 7459 Avenue Hippocrate, B-1200 Brussels, Belgium
Eur J Immunol; 12(5):401-406 1982

The cytolytic T lymphocyte (CTL) response of syngeneic mice to antigenic variants obtained by mutagenesis of mastocytoma P815 was analyzed at the clonal level. Estimates of the frequency of CTL precursor cells in spleens from mice immunized with P815 variants ranged from 10(-4) to 2 x 10(-3). This frequency could be increased approximately 100x by stimulating immune spleen cells in mass culture for 6-8 days with the immunizing variant. Specificity analysis of a large number of individual CTL clones demonstrated the existence of two distinct populations of CTL. Some CTL clones lysed exclusively the immunizing variant, while others lysed equally well all P815 targets, but not syngeneic tumor L1210. These results provide direct evidence for the existence of new, individual specificities on P815 variants in addition to a common antigen already present on the original P815 cells. This confirms that a variety of new antigens can be induced by mutagenesis on the same background cells. Stable, highly active CTL clones specific for either individual variant antigens or common P815 antigens could be maintained in long-term culture. (Author abstract) (26 Refs)

23. IMMUNOGENIC VARIANTS OBTAINED BY MUTAGENESIS OF MOUSE MASTOCYTOMA P815: IV. ANALYSIS OF VARIENT-SPECIFIC ANTIGENS BY SELECTION OF ANTIGEN-LOSS VARIANTS WITH CYTOLYTIC T CELL CLONES.

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Eur J Immunol; 12(5):406-412 1982

Mouse mastocytoma P815 tumor cell variants that express new individual antigens were subjected to immunoselection in vitro with specific cytolytic T lymphocyte (CTL) clones. From one variant (P35) a number of resistant clones were isolated after a single-step selection. These immunoselected clones (P35 iscA-) proved to have acquired a stable and complete resistance to lysis by the selecting CTL, but remained sensitive to lysis by a CTL clone that recognizes a common P815 antigen. However, when these P35 iscA- clones were used to stimulate in vitro spleen cells from mice immunized with variant P35, the cytolytic activity was significantly higher on P35 and P35 iscA- targets than on the original P815 clone (P1). This indicated that P35 iscA- cells, which had lost a P35-specific determinant (P35A), had nevertheless retained another P35-specific determinant (P35B). CTL clones directed against the residual P35B determinant were then isolated. When P35 cells were submitted to selection with anti-P35B CTL, resistant clones (P35 iscB-) were obtained that were still lysed by anti-P35A and anti-P815 CTL clones. Tum- variant P35 therefore carries at least two specific determinants that can be lost independently. These results show the possibility of using selection with CTL clones to separate different components of complex cell surface antigens. The correlation between antigen expression and tumorigenicity was also examined. Antigen-loss P35 iscA- clones were found to be more tumorigenic than variant P35 which has a greatly reduced tumorigenic capacity compared to the original P815 tumor. This correlation suggests that the P35 determinant that was no longer expressed by the P35 iscA- clones is recognized on the original P35 tum- variant as a tumor rejection antigen. (Author abstract) (21 Refs)

24. MONOCLONAL T CELL HYBRIDOMA THERAPY OF MOUSE INTESTINAL GRANULOMATOUS LESIONS (MEETING ABSTRACT).

Ginsburg CH, Takaoki M, Dambrauskas JT, Falchuk ZM, Whitaker B, Greene MI
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Gastroenterology; 82(5,part2):1067 1982

The ability of a thymus-derived (T cell) hybridoma product to inhibit granulomatous lesions was studied in mice to develop a model in which the effect of immune therapy might be assessed. It is possible to achieve suppression of antigen-specific immune responses using appropriately generated suppressor cells (Ts). Antigen-specific T-cell suppression in the murine species proceeds, in a genetically restricted manner, by a common pathway involving the sequential induction of distinct T-cell subsets (Ts1, Ts2, Ts3). The Ts1 and Ts2 subsets produce specific factors (TsF) which activate the next Ts in the pathway. We generated Ts2 cells in A/J mice by the administration of a well-characterized antigen specific long-term Ts1 cell hybridoma product (monoclonal TsF). The Ts2 cells were transferred into syngeneic antigen-primed mice at the time of challenge and at 24-hour intervals after challenge with antigen-coupled polyacrylamide beads into the intestinal wall. Since we previously showed that antigen-specific granulomas form after such challenge, bead-injection sites were assessed histologically for granulomas. Transfer of Ts2 to primed mice at the time of challenge and 24 hours post challenge resulted in complete suppression of granulomas. Primed mice not receiving Ts2 or those receiving control factors developed granulomas by 72 hours post challenge. Furthermore, the ability of Ts2 to inhibit granulomas only when given up to 24 hours after challenge suggests that either immunological events relevant to granuloma formation happen early after challenge, or that later events are not regulated in this manner. (1 Ref)

25. INDUCTION OF ANTERIOR CHAMBER-ASSOCIATED IMMUNE DEVIATION (ACAID) BY ALLOGENEIC INTRAOCULAR TUMORS DOES NOT REQUIRE SPLENIC METASTASES.

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J Immunol; 128(6):2470-2474 1982

Anterior chamber-associated immune deviation (ACAID), induced by intracameral injection of allogeneic tumor cells, is expressed in three distinct ways: (1) progressive growth of intraocular tumors, (2) specific suppression of systemic allograft immunity, and (3) transient growth of allogeneic tumors injected sc. Induction of ACAID requires that alloantigen presentation occur via the anterior chamber; injection by other routes failed to elicit this phenomenon. Antigenic material must remain in the anatomically intact eye for at least 10 days; removal of the injected dye before this time prevented the establishment of ACAID. The similar temporal requirement for an anatomically intact spleen confirms the validity of the concept of a camero-splenic axis for processing of intracamerally injected alloantigens. Deployment of an alternate model of ACAID, using LP/J mice injected intracamerally with B16F10 melanoma, showed the antigen-specific inductive signal for ACAID (transmitted via the camero-splenic axis) was not in the form of viable alloantigen-bearing tumor cells that metastasize to the spleen. B16F10 melanoma cells were never found in the spleens or any other extraocular sites after intracameral injection, despite the fact these mice manifested ACAID and harbored enormous ocular tumors. The data emphasize that intraocular processing of antigens is a unique and dynamic phenomenon with significant, systemic immunologic consequences (Author abstract) (18 Refs)

VIRUS ASSOCIATED ANTIGENS

26. HUMAN LYMPHOMA-LYMPHOMA HYBRIDS AND LYMPHOMA-LEUKEMIA HYBRIDS. II. EPSTEIN-BARR VIRUS INDUCTION PATTERNS.

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JNCI; 68(2):197-202 1982

In addition to the spontaneous expression of markers of the early and late phases of the viral cycle [Epstein-Barr virus (EBV), early viral cycle antigens (EA), and viral capsid antigen (VCA)] by a panel of hybrid cell lines derived by fusion of human hematopoietic cell lines, the induction of these markers by three chemical inducers [5-iodo-2'-deoxyuridine, the tumor promoter 12-O-tetradecanoylphorbol 13-acetate (TPA), and sodium butyrate] were analyzed. A variant of the prototype producer of lytic EBV, P3HR-1 (PICAT) was observed to show consistent low spontaneous and induced production of EA and VCA as compared to the P3HR-1 line from which it was derived. An 'autohybrid' (PICATPO-1) between these two lines showed a low production of VCA. Hybrids between Raji and P3HR-1 sublines (RUD-PICAT-1 and RUDPUT-2) showed reduced expression of EBV antigens. Both hybrids were capable of VCA expression, in contrast to the Raji parent that expressed EA but not VCA. A new Raji-Daudi hybrid (DITRUD-1) expressed spontaneous and induced EA and VCA at levels intermediate between its two parents. A different type of hybrid was derived from a Daudi subline and the K562 leukemia cell line (DUTKO-1) and was found to be capable of spontaneous as well as induced EA and VCA expression. Both DUTKO-1 and DITRUD-1 were similar to Daudi in their induction profile in respect to a very low response to TPA. (Author abstract) (20 Refs)

27. A HUMAN HEPATOMA CELL LINE (PLC/PRF/5) PRODUCES LUNG METASTASES AND SECRETES HBSAG IN NUDE MICE.

Sattler FR, Paolucci S, Kreider JW, Ladda RL
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Eur J Cancer Clin Oncol; 18(4):381-389 1982

PLC/PRF/5 is a human liver cancer cell line which synthesizes hepatitis B virus surface antigen (HBsAg). These cells produced tumor in 6 of 8 (75%) congenitally athymic nude mice at 13 of 28 subcutaneous injection sites and in 13 of 14 (93%) mice inoculated intraperitoneally. Tumors were successfully transplanted to four of six additional nude mice. Tumor growth was rapid. Growth of cephalad tumors was significantly greater than for caudal tumors (0.39 mm/day vs 0.28 mm/day). Microscopic examination of tumors showed moderately well-differentiated hepatocellular carcinoma. Foci of identical cells were present in pulmonary veins in 7 of 14 tumor-bearing animals. Tumor cell karyotype was identical with that of PLC/PRF/5 cells. In addition, HBsAg was detectable in high titer in animals with extensive tumor. Biological features of PLC/PRF/5-induced tumors in nude mice appeared to closely resemble human hepatocellular carcinoma. Moreover, HBsAg may provide a marker of tumor growth. (Author abstract) (24 Refs)

28. HEPATITIS-B VIRUS INFECTION IN BLACK CHILDREN WITH HEPATOCELLULAR CARCINOMA.

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Dept. Medicine, Witwatersrand Univ. Medical Sch., Hospital Hill, Johannesburg 2001, South Africa
J Med Virol; 9(3):201-207 1982

Six unselected South African black children (2 female, 15 and 16 yr old; 4 male, 10-13 yr old) with hepatocellular carcinoma (HCC) were examined for hepatitis-B virus (HBV) infection. Characteristics of the tumors were similar to those in black adults. All of the patients were positive for hepatitis B surface (HBs) antigen and hepatitis B core antigen in the serum. Hepatitis Be antigen was present in four patients; sera from the two patients without e antigen (1 male, 1 female) were positive for e antibody. All of the sera were negative for HBs antigen. Taken in conjunction with the HBV status of black adults in South Africa, the findings suggest the possibility that nearly all black patients with HCC are or have been infected with HBV. If HBV is oncogenic, tumor formation may occur within 10 yr of the initial infection. (14 Refs)

29. EVIDENCE THAT HEPATITIS B VIRUS HAS A ROLE IN LIVER-CELL CARCINOMA IN ALCOHOLIC LIVER DISEASE.

Brechot C, Nalpas B, Courouce AM, Duhamel G, Callard P, Carnot F, Tiollais P, Berthelot P
Unite de Recombinaison et Expression Genetique, Institut Pasteur, 28 rue du Docteur Roux, 75015 Paris, France
N Engl J Med; 306(23):1384-1387 1982

Determinations of hepatitis B virus (HBV) DNA were made in a prospective study of 51 alcoholics without hepatocellular carcinoma (HCC) and in a retrospective study of 20 alcoholics with both alcoholic cirrhosis and HCC. The overall prevalence of HBV serologic markers was 37% in the first group, compared with 10% in a nonselected blood-donor population. HBV DNA was detected in liver samples from three hepatitis B surface antigen (HBsAg)-positive patients from the first group and in liver samples of five other patients from this group in whom serum HBsAg was not detectable. In the second group, HBV DNA was detected in the neoplastic portion of the autopsied liver in all patients. Integration of viral DNA into the hepatocellular DNA was demonstrated in the samples from the second group, but conclusively in only two samples from the first group. HBV DNA was not detected in the livers of 14/16 patients with alcoholic liver disease (from the first group) who were negative for HBsAg but positive for anti-hepatitis B core antigen or anti-HBsAG, suggesting that HBV is probably not involved in progression of the liver disease. The presence of HBV DNA in livers of alcoholic patients without HCC may delineate the population at high risk for development of this disease. (25 Refs)

30. CLINICAL AND IMMUNOLOGICAL ASPECTS OF HEPATITIS B VIRUS INFECTION IN CHILDREN WITH HAEMATOLOGICAL MALIGNANCIES.

Koscielniak E
Dept. Hematology, Pediatric Clinic, Medical Acad., Wronskiego 11, 50-372 Wroclaw, Poland
Arch Immunol Ther Exp (Warsz); 29(5):689-695 1981

One hundred forty three patients with hematological malignancies were screened at the onset and during the disease for hepatitis B surface antigen (HBsAg) in the serum. HBsAg was found in serum of 38/143 patients (26.5%) in a mean period of 14.5 mo after the diagnosis was established. The relationship between immunological status of the patients and the course of the infection was analyzed. In 17/38 patients who developed icteric hepatitis, the mean amounts of E-rosetting lymphocytes were significantly higher than in the anicteric hepatitis group and asymptomatic HBsAg carriers. These two groups of patients showed a tendency to persistence of HBsAg and developing of chronic carrier state or chronic hepatitis. (Author abstract) (19 Refs)

31. DIFFERENT PAPILLOMAVIRUSES AS THE CAUSES OF ORAL WARTS.

Lutzner M, Kuffer R, Blanchet-Bardon C, Croissant O
Unite des Papillomavirus, Institut Pasteur, 25 rue du Docteur Roux, 75724 Paris 15, France
Arch Dermatol; 118(6):393-399 1982

We have observed four patients with oral papillomas. Two children had oral mucosal lesions characteristic of focal epithelial hyperplasia, a young man had common, wart-like lesions on his hard palate, and a male immunosuppressed renal allograft recipient had condyloma-like lesions on his gingivae. Papillomavirus-like particles were seen by electron microscopy in lesions from both patients with focal epithelial hyperplasia. No structural antigens for human papillomavirus (HPV) 1, 2, 3, or 5 were found by immunofluorescent microscopy, but further evidence of the presence of a papillomavirus was found by immunoperoxidase microscopy using a cross-reacting sodium lauryl sulfate-disrupted bovine papillomavirus 1 anti-rabbit serum sample. The distinct histologic pattern seen in focal epithelial hyperplasia suggests that a yet undescribed HPV type might be associated with this disease. Histologic, ultrastructural, and immunofluorescent microscopy and restriction endonuclease analysis all gave evidence of HPV 2 in the palatal lesions in patient 3. Evidence of papillomavirus antigen was found by immunoperoxidase microscopy in the oral condylomas from our immunosuppressed patient. (Author abstract) (31 Refs)

32. DEMONSTRATION OF PAPILLOMAVIRUS ANTIGEN IN PARAFFIN SECTIONS OF LARYNGEAL PAPILLOMAS.

Braun L, Kashima H, Eggleston J, Shah K
Dept. Pathobiology, Johns Hopkins Univ. Sch. Hygiene and Public Health, 615 North Wolfe St., Baltimore, MD, 21205
Laryngoscope; 92(6,part1):640-643 1982

A papillomavirus antigen has been identified in tissue sections of laryngeal papillomata removed at endoscopic operations. The demonstration of the papillomavirus antigen was achieved using the peroxidase-antiperoxidase test of Sternberger after a broadly cross-reactive rabbit antiserum to the papillomavirus capsid antigen was incubated with the tissue sections. The antigen was detected in specimens from 7 of 15 patients with juvenile-onset laryngeal papillomas, but could not be demonstrated in the specimens from six patients with adult-onset papillomas. In all, 73 biopsy specimens from 21 patients were selected for study; 18% (11/61) of the sections from the juvenile-onset patients and 0% (0/12) of the sections from the adult-onset patient specimens exhibited the papillomavirus antigen. The presence of the virus antigen did not correlate with the stage of disease, nor with the duration or severity of the illness. The implications of the findings are discussed. (Author abstract) (17 Refs)

TUMOR ASSOCIATED TRANSPLANTATION ANTIGENS

33. NATURAL AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY IN TUMOR-ADHERENT T LYMPHOCYTES: EXPRESSION OF FC RECEPTORS AND OF A HUMAN T-SUBGROUP-SPECIFIC ANTIGEN.

Feucht HE, Hadam MR, Lohmeyer J, Frank F, Rieber EP, Riethmuller G
Medical Clinic, Univ. Munich, Ziemssenstr. 1, D-8000 Munich 2, W. Germany
Scand J Immunol; 15(5):483-492 1982

Adherence of human lymphocytes to allogeneic tumor cell monolayers was found to depend on the presence of monocytes. Adherent lymphocytes could be separated from tumor cells by treatment with lidocaine followed by nylon wool passage. Tumor-adherent cells (70% E-RFC, 45% Fcgamma-R, 23% Fcu-R, 5% monocytes) exhibited enriched natural killer (NK) activity not only against the tumor cell line used for isolation but also against seven other targets. When T cells were isolated subsequently as E-rosettes by density gradient centrifugation through Percoll, the enrichment in cytotoxicity was even more pronounced. Tumor-adherent T cells were several-fold enriched in both NK and antibody-dependent cell-mediated cytotoxicity (ADCC) activity. However, this enrichment was not paralleled by a concomitant increase in the number of Tgamma cells (tumor-adherent T cells: 17% Tgamma, 40% Tmu; tumor-nonadherent T cells: 12% Tgamma, 60% Tmu). Marked differences could be observed by staining with a monoclonal antibody that was raised against human leukemic Tgamma cells of high NK and ADCC activity. This antibody (T 8-11) stained 60% of tumor-adherent T cells, 20% of nonadherent T cells and 29% of T-cell controls. These results indicate that the spontaneous cytotoxic activity of human T cells resides within a small population, most of which are characterized by a specific surface antigen but not by conventional Fcgamma receptors. (Author abstract) (41 Refs)

34. POSSIBLE ROLE OF A RETROVIRUS IN THE EXPRESSION OF TUMOR-SPECIFIC ANTIGENS OF THE METH A SARCOMA.

DeLeo AB, Chang KS, Wivel NA, Appella E, Old LJ, Law LW
Sloan-Kettering Cancer Center, New York, NY
Int J Cancer; 29(6):687-693 1982

The serologically defined tumor-specific surface antigen (TSSA) of the chemically-induced BALB/c Meth A sarcoma, highly restricted to 1 of 20 sarcomas of BALB/c origin, has been detected on a Moloney murine sarcoma virus (MoMuSV)-transformed BALB/c3T3 cell line, designated 11A(v). The immunogenicity of the 11A(v) cell in tumor-rejection assays was specific for the Meth A sarcoma, supporting the evidence for a close relationship between the TSSA and the tumor-associated transplantation antigen (TATA) of this tumor. Infection of SC-1 cells with retroviruses present in cultured filtrates of IIA(v) cells resulted in Meth A antigen expression. The retroviruses associated with Meth A antigen expression have been tentatively identified as replication and/or transformation-defective XC-MuLV. The possible roles of MoMuSV and cellular genes of the BALB/c strain of mice in the expression of the Meth A antigen are discussed. (Author abstract) (43 Refs)

CLINICAL DIAGNOSTIC STUDIES

35. IN VIVO RADIOIMMUNOLOGICAL LYMPHOSCINTIGRAPHY IN CANCER. THE IMPLICATIONS OF POSITIVE FINDINGS.

Deland FH, Goldenberg DM
Dept. Nuclear Medicine, Univ. Kentucky, Albert B. Chandler Medical Center, Lexington, KY, 40536
J Can Assoc Radiol; 33(1):4-9 1982

Radionuclide-labeled antibodies to tumor-associated antigens were applied to the detection of the lymphatic spread of carcinoma by the technique of lymphoscintigraphy. In women with proven carcinoma of the breast, all of whom had clinical or surgically proven axillary metastases, 100% of metastases were detected by gamma imaging. In three cases of squamous cell carcinoma of vulva, one with bilateral inguinal metastases, one with ipsilateral metastases, and one with no metastases, imaging revealed that I-131 labeled antibodies were sequestered bilaterally in the inguinal lymph nodes of all three patients. Submucosal injections of the uterine cervix with labeled antibodies were performed in patients with carcinoma of the cervix, and again sequestration of radioactivity was detected in pelvic nodes. Subsequent hysterectomy with lymph node dissection revealed high levels of radioactivity in specific lymph nodes but no evidence of metastatic tumor. In view of previous work by Nossal and his group, we speculate that the sequestration of the antibody was based on trapping of the antigen by the lymph nodes, and an antibody-antigen reaction on the surface of cells within the nodes. To prove this hypothesis, appropriate animal experiments were performed. The detection of antigen trapping may have important implications in the diagnosis and therapy of cancer. (Author abstract) (37 Refs)

36. MONOCLONAL ANTIBODIES REACTIVE WITH HUMAN MYELOID LEUKAEMIA CELLS.

Ball ED, Fanger MW
Dept. Microbiology, Dartmouth Medical Sch., Hanover, NH, 03755
Clin Exp Immunol; 48(3):655-665 1982

Hybridomas producing monoclonal antibodies that bind to determinants on myelogenous leukemia blast cells were developed using fresh leukemia blasts as immunogens. These monoclonal antibodies were used to quantitate the amount of a variety of antigens on both leukemia and normal blood cells in a radioimmunoassay. The ability of these antibodies to mediate complement-dependent lysis of leukemia cells and normal blood cells was evaluated. Significant quantitative differences in the expression of a variety of cell surface antigens were observed among different myeloid leukemia cell samples, normal cells, and other forms of leukemia. However, none of the monoclonal antibodies studied were found to be specific for myeloblasts. Despite the fact that these antibodies bound to both leukemia and normal cells, several of them mediated complement-dependent cytotoxicity which was restricted to leukemic myeloblasts (AML-1-211, AML-2-30, CML-18, CML-75, CML-115, and CML-150). None of these clones, alone or in any combination, were capable of lysing normal lymphocytes or monocytes. Others were specifically cytotoxic to leukemia cell lines (AML-1-99). B cells and some leukemia samples (AML-2-9), and myelomonocytic leukemia cell samples and normal monocytes (AML-2-23). Several of the monoclonal antibodies from this panel appear to be promising for future clinical applications. (Author abstract) (32 Refs)

37. ANTIBODIES TO ADULT T-CELL LEUKEMIA-VIRUS-ASSOCIATED ANTIGEN (ATLA) IN SERA FROM PATIENTS WITH ATL AND CONTROLS IN JAPAN: A NATION-WIDE SERO-EPIDEMIOLOGIC STUDY.

Hinuma Y, Komoda H, Chosa T, Kondo T, Kohakura M, Takenaka T, Kikuchi M, Ichimaru M, Yunoki K, Sato I, Matsuo R, Takiuchi Y, Uchino H, Hanaoka M
Inst. Virus Res., Kyoto Univ., Kyoto 606, Japan
Int J Cancer; 29(6):631-635 1982

A nation-wide sero-epidemiologic survey of adult T-cell leukemia virus (ATLV), detected as anti-ATLA (ATLV-associated antigen), was made in Japan. Sera from adult donors in 15 different locations were screened for anti-ATLA. High incidences (6 to 37%) of antibody-positive donors were found in seven regions, one in northern Japan, and the others in southwestern regions. These areas are ATLV-endemic areas corresponding to ATL-endemic areas. Examination of sera from healthy donors aged 6 to 80 yr in ATL-endemic areas showed an age-dependent increase of seropositive donors with a maximum of about 30% to 40 yr of age. Anti-ATLA was found in all but two of 142 patients with ATL. Anti-ATLA-positive patients with ATL were mainly found in ATLV-endemic areas and only a few in ATL-nonendemic areas. Six patients with cutaneous T-cell lymphoma in ATLV-nonendemic areas gave a negative reaction for anti-ATLA. The geometric mean titer of anti-ATLA of patients with ATL was higher than that of healthy donors. (Author abstract) (9 Refs)

38. UTILITY OF MONOCLONAL ANTIBODIES IN THE IMMUNOLOGIC PHENOTYPING OF ACUTE LYMPHOBLASTIC LEUKEMIA.

Yu AL, Royston I, Leung KL, Kung FR, Hartman GA, Lightsey AL, Vangrove J, Sobol RE
(c/o Royston) Div. Hematology/Oncology, V-111E, Dept. Medicine, Univ. California San Diego Sch. Medicine, 3350 La Jolla Village Drive, La Jolla, CA, 92161
Hybridoma; 1(2):91-98 1982

Two monoclonal antibodies were used in conjunction with conventional lymphocyte markers to characterize acute lymphoblastic leukemia (ALL) in 34 children and 11 adults. Monoclonal antibody T101 detects a 65,000 mol wt cell surface antigen (T65) found on all T-cells in the peripheral blood and lymph node, T-cell lines, and thymocytes; the second antibody detects a monomorphic determinant on the Ia-like antigen, which is a bimolecular complex of 27,000 and 35,000 mol wt. Four distinct phenotypes were evident in the childhood ALL patients; the most common of these was observed in 22 patients. The marker profiles of the 11 adult patients exhibited the four phenotypes found in the childhood cases, and one additional phenotype. The most common phenotype, found in 6/11 patients, was the same as the most common phenotype in the childhood group. Reactivity with monoclonal anti-Ia and anti-T65 antibodies appears to define two distinct clinical subgroups of childhood ALL. The more common group was Ia + T65-and was characterized by an equal male:female distribution; younger age, lower leukocyte count, and lower incidence of organ involvement at presentation; and longer disease-free survival than Ia-T65 + patients. The less common Ia-T65 + group was associated with male predominance, anterior mediastinal mass, high leukocyte count, organ involvement, and early treatment failure. Anti-Ia and T101 reactivity are apparently mutually exclusive in ALL, since no Ia + T65 + patients were identified. (24 Refs)

39. CHRONIC LEUKEMIA WITH A HYBRID SURFACE PHENOTYPE (T LYMPHOCYTIC/MYELOMONOCYTIC): LEUKEMIC CELLS DISPLAYING NATURAL KILLER ACTIVITY AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY.

Schlimok G, Thiel E, Rieber EP, Huhn D, Feucht H, Lohmeyer J, Riethmuller G
Medical Clinic II, Langemarckstr. 11, 8900 Augsburg, W. Germany
Blood; 59(6):1157-1162 1982

A patient with chronic leukemia exhibited uncommon clinical features, such as hypergammaglobulinemia and activation of intravascular coagulation after low-dose irradiation of the enlarged spleen. By light and electron microscopy, the leukemic cells resembled large granular lymphocytes. The following markers were simultaneously expressed on their surface: receptors for sheep erythrocytes and the Fc part of IgG; common T-cell antigens as revealed by a heteroantiserum (HuTLA) and monoclonal antibodies (OKT3, T411); antigens shared by cytotoxic/suppressor T cells (OKT8, T811) as well as myelomonocytic antigens defined by the OKM1 and M522 monoclonal antibodies. The leukemic cells showed both spontaneous (NK) and antibody-dependent (ADCC) cytotoxicity, but they did not suppress B-cell differentiation in vitro. (Author abstract) (40 Refs)

40. SURFACE ANTIGENIC PHENOTYPES OF HUMAN T-CELL LEUKEMIA CORRESPONDING TO THOSE OF POST-THYMIC T CELLS.

Ishii Y, Fujimoto J, Kon S, Ogasawara M, Koshiba H, Mikuni C, Kikuchi K
Dept. Pathology, Sapporo Medical Coll., S1 W17, Sapporo 060, Japan
Am J Hematol; 12(3):251-260 1982

Leukemic cells from eight adult patients with various types of T-cell leukemias, including one patient with lymphosarcoma cell leukemia (T-LSL), two patients with chronic lymphocytic leukemia (T-CLL), and five patients with adult T-cell leukemia (ATL), were analyzed for their surface antigenic phenotypes with a series of monoclonal antibodies directing to human T-cell differentiation antigens. All of the leukemic T cells studied were regarded as being of post-thymic T-cell origin because of their ability to form rosettes with sheep red cells under the condition at 4 C but not 37 C as well as the expression of human Ly-1-like but not TL-like antigen on their cell surfaces. By using monoclonal antibodies to a variety of human T-cell antigens (Leu-1, Leu-2a, and Leu-3a), all eight cases could be divided into either group of three distinct categories. Thus, one patient with T-LSL had cells with Leu-1+2a+3a+ phenotype, which might reflect possible post-thymic precursor T cells, whereas one patient with T-CLL had cells with the same phenotype (Leu-1+2a+3a-) as normal cytotoxic/suppressor T cells. The latter cells also expressed Ia antigens as defined by monoclonal anti-human Ia antibody. The remaining six cases, including one T-CLL and five ATL patients, had leukemic cells with the same phenotype (Leu-1+2a-3a+) as normally found on helper/inducer T cells, despite distinct clinical and immunological features between T-CLL and ATL. Some clinical findings observed in those patients may reflect functional activities retained by their leukemic T cells. (Author abstract) (34 Refs)

41. HETEROGENEITY OF MELANOMA-ASSOCIATED ANTIGENS DETECTED BY SERA FROM PATIENTS RECEIVING ADJUVANT ALLOGENEIC TUMOR VACCINE IMMUNOTHERAPY.

Dent PB, McCulloch PB, Liao SK, Stone BR, Singal DP
Dept. Pediatrics, Internal Medicine and Pathology, McMaster Univ., Ontario Cancer Treatment and Res. Foundation, Hamilton Clinic, Hamilton, Ontario L8N 3Z5, Canada
Clin Immunol Immunopathol; 23(2):379-391 1982

Sera from 40 patients with malignant melanoma entered into a randomized controlled trial of nonspecific and specific active immunotherapy were studied for the presence of melanoma-specific IgG antibody. Reactivity was revealed by mixed hemadsorption assay against a panel of 10 cultured melanoma cell lines. Prior to therapy 3 of 40 patients had antibody to one or more melanoma lines which in all cases was eliminated by absorption with platelets or colon carcinoma cells. After 6 mo of therapy patients in the group not receiving tumor vaccine had no absorption-resistant antimelanoma reactivity. However all 10 patients receiving allogeneic tumor vaccine had high titered melanoma reactivity which in 8 patients was not removed by platelet or carcinoma absorption. Three patients reacted only against melanoma targets while of the remaining five patients, four reacted against cultured brain tumor cells supporting previous suggestions of a possible antigenic cross-reactivity among tumors of neuroectodermal origin. Clinical outcome was not correlated with the presence of antibody to melanoma target cells. Persistance of antibody was dependent on continued vaccine administration suggesting that rather than being an index of resistance, the presence of antibody may be a marker for the presence of tumor. Sera from alloimmunized melanoma patients identify a heterogeneous complex of melanoma-associated surface antigens. More information about the serological and immunological properties of these antigens is required to determine if these responses are clinically relevant. (Author abstract) (21 Refs)

42. FLOW CYTOFLUOROMETRIC DETECTION OF TUMOR-SPECIFIC ROSETTE-FORMING CELLS IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK.

Tong AW, Vandenbark AA, Kraybill W, Vetto RM, Burger DR
Dept. Microbiology, Oregon Health Sciences Univ., Portland, OR, 97207
Cancer Res; 42(7):2949-2955 1982

Tumor-specific rosette-forming cells reactive to solubilized tumor antigens conjugated to autologous erythrocytes were quantitated by flow cytofluorometry. Leukocytes from a high frequency of the patients (greater than 70%) with squamous cell carcinoma of the head and neck (SQCC) formed rosettes to the conjugated SQCC tumor antigens but not to other histologically distinct tumor antigens (melanoma and colon carcinoma). Healthy control subjects or tumor patients with other cancers were mostly unreactive to the SQCC tumor extract [1 of 21 (5%) and 1 of 14 (7%) for controls and tumor patients, respectively]. Rosette-forming activity was observed in SQCC patients with primary cancers [22 of 30 (73%)] or in remission [5 of 6 (83%)], whereas patients with tumor recurrence were uniformly unresponsive. Tumor-specific rosette formation was mediated predominantly by monocytes, as identified by histochemical techniques and physiological properties. Rosette formation in reactive patients was abrogated by short-term culture, but the abated response could be restored by incubation with autologous serum or sera from other rosette-forming cell-positive patients. However, responsiveness of nonreactive patients with SQCC recurrence could not be constituted by rosette-forming cell-positive sera. These observations suggested the presence of tumor-reactive monocytes in a high frequency of patients with primary cancer or in remission but not in patients with recurrent disease. (Author abstract) (28 Refs)

43. LEWIS BLOOD-TYPE MAY AFFECT THE INCIDENCE OF GASTROINTESTINAL CANCER.

Koprowski H, Blaszczyk M, Steplewski Z, Brockhaus M, Magnani J, Ginsburg V
Wistar Inst., 36th St. at Spruce, Philadelphia, PA, 19104
Lancet; 1(8285):1332-1333 1982

The frequency of gastrointestinal cancer antigen (GICA) was studied in the sera of 315 patients with gastrointestinal cancer (GIC), of 89 patients with other malignancies, and of 108 healthy subjects, and on tumor cells from some of the GIC patients. Sera of 64% of the patients with clinically and histologically proven colorectal cancer, 92% of patients with pancreatic cancer, and 72% of patients with gastric cancer inhibited binding of anti-GICA monoclonal antibody to GICA-containing cancer cells. Sera of 8% of patients with malignancies other than GIC and 2% of healthy subjects inhibited binding. Among the eight patients with tumors other than GIC whose sera inhibited binding of the antibody, three had liver carcinoma. GICA was expressed in 55% of the colorectal cancer tissue samples, in 82% of pancreatic cancer tissues, and in

100% of gastric cancer tissues. Cells of 1/8 liver carcinomas and 1/5 gallbladder carcinomas were positive for GICA. The relationship of Lewis blood type to GIC and GICA expression is discussed. (14 Refs)

44. BLOOD GROUP PRECURSOR T-ANTIGEN EXPRESSION IN HUMAN URINARY BLADDER CARCINOMA.

Coon JS, Weinstein RS, Summers JL
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Am J Clin Pathol; 77(6):692-699 1982

Tumor deletion of the ABH blood group antigens (BGAg) heralds an unfavorable prognosis in human bladder cancer. The T antigen (Thomsen-Friedenreich antigen: TAg), a precursor of other BGAg, has previously been found in malignant but not most normal cells, in which the TAg is cryptic but can be unmasked with neuraminidase (NMD). We investigated the prognostic significance of TAg expression in bladder cancer by staining paraffin sections with a T-specific lectin (peanut agglutinin [PNA]) immunoperoxidase technic. Seventy-two cases of low grade, low stage bladder cancer, 21 cases of high grade bladder cancer, and 68 controls were studied. All normals expressed the TAg only after NMD treatment (Cryptic TAg+). The Grade III cancers, all invasive, either expressed the TAg (TAg+) (67%) or lacked T even after NMD (Cryptic TAg-) (29%), indicating that the T structure was lost rather than masked as in normal tissue. Thirty-nine percent of 23 Grade I and II cancers which were TAg+ or Cryptic TAg- subsequently became invasive (Stage B), compared with 10% of 49 Cryptic TAg+ cancers. For 32 Grade I and II, ABH BGAg negative cancers, 64% of TAg+ or Cryptic TAg- cancers became invasive, compared with 17% of cancers which had Cryptic TAg+. Thus, the TAg may be a prognostically useful immunohistochemical tumor marker in bladder cancer, especially for tumors negative for ABH BGAg. (Author abstract) (37 Refs)

45. BLOOD GROUP ABO (H) CELL SURFACE ANTIGENS IN BLADDER TUMORS INVADING THE CHORION. PROGNOSTIC VALUE OF THEIR DETERMINATION BY IMMUNOFLUORESCENCE. RETROSPECTIVE STUDY OF ONE HUNDRED AND TWENTY-FIVE CASES.

Vacant J, Le Portz B, Augustin I, Hammou JC, Fella C, Delignieres S, Maiolini R, Masseyeff R, Abelanet R, Steg A
GRET, G.I.E. FAX, 5, rue Eugene Emmanuel, 06000 Nice, France
Sem Hop Paris; 58(21):1295-1300 1982

The authors have studied 125 Stage A bladder tumors with a follow-up period of at least 5 yr. The ABH cell surface antigens were collected by a double-layer immunofluorescence technique which has already been described. All the cross sections were read by the same pathologist who knew nothing about the clinical developments. The results were divided into 3 groups: (I) all the tumor cells had retained their surface antigens. (II) Only some cells had retained surface antigens. (II) All cells were negative. Study of the development of the three groups shows that: in Group I, all the patients (11) are alive 5 yr later, and only one has presented with a lesion evolving towards infiltration. In Group II (32 patients), only 38% of the patients are still living 5 yr later, and 65% developed towards muscular infiltration. In Group III (77 patients), 27% are alive after 5 yr and 80% have developed towards muscular infiltration. Homogeneous retention of the surface antigens would therefore seem to be a favorable factor in the prognosis, even in the case of a tumor which has already infiltrated the chorion. The significance of the loss of surface antigens is less clear-cut, but is on the whole adverse. The significance would, however, probably be enhanced by study of the mucosa distal from the lesion, and by marking the substances which determine the blood groups. (Author abstract) (27 Refs) (In FRE)

46. DETECTION OF CIRCULATING TUMOUR-ASSOCIATED ANTIGENS IN SERUM OF WOMEN WITH CERVICAL NEOPLASIA. USE OF RABBIT ANTISERUM TO A CONTINUOUS CANCER CELL LINE (C-4111).

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Br J Obstet Gynaecol; 89(3):238-240 1982

Hyperimmune rabbit sera to partially purified human cervical cancer tissue antigen (CaCxTAA) and to human cervical cancer culture cell line antigens (C-4II-TAA) were used to demonstrate circulating tumor-associated antigens (C-TAA) in the sera of women with cervical neoplasia. Rabbit anti-CaCx serum detected C-TAA in 80% of the 60 sera from women with invasive cancer, cancer in situ and severe dysplasia and the rabbit anti-C-4II serum detected 67% of these cases. Negative reactions were obtained in over 95% of the 154 control sera with either rabbit serum. These results suggest that, in view of the difficulty of obtaining large specimens of cervical cancer tissues for the development of immunodiagnostic procedures, the use of a cervical cancer cell line, such as C-4II, appears desirable. Such cell lines would also be advantageous for studies aimed at providing further support for the association between genital herpes simplex virus infection and human cervical cancer. (Author abstract) (10 Refs)

47. LEVELS OF CIRCULATING IMMUNE COMPLEXES IN PATIENTS WITH OVARIAN CANCER.

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Br J Obstet Gynaecol; 89(3):231-237 1982

Sera from patients with ovarian tumors were assayed for circulating immune complexes (CIC) by four well established assays based on the interaction of immune complexes with components of the complement system. There was no difference in control, pre- or post-operative or BCG-treated patients' sera. Levels were also unchanged in sera in antigen excess. In patients with ovarian tumors before the measurement of CIC would appear to be of little value as a screening test, as a guide to the extent of disease, prognosis or therapy. In a small pilot therapy-trial there was no difference in the survival rate between patients with Stage III and IV ovarian cancer treated with cyclophosphamide plus BCG and those who received only cyclophosphamide. Treatment with BCG was associated with postoperative pyrexia and a prolonged hospital stay. (Author abstract) (43 Refs)

48. REACTIVITY OF HUMAN LYMPHOCYTES TO TERATOMA PREPARATIONS AS REVEALED BY THE MACROPHAGE ELECTROPHORETIC MOBILITY (MEM) TECHNIQUE.

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Arch Geschwulstforsch; 52(5):349-353 1982

Reactivity of lymphocytes from cancer patients to extracts of teratoma tissues was studied by means of the macrophage electrophoretic mobility (MEM) test. Metastastic tissue of a malignant mediastinal teratoma in a young man and tissue of a malignant abdominal teratoma in a girl were used. Both teratomas contained elements of all three germ layers. Extracts were made using 3 M KCl. Lymphocytes were obtained from 119 patients with various types of cancers, 46 healthy controls, and 47 patients with benign diseases. Samples of 10(6) lymphocytes were incubated with 200 ul of extract for 90 min at 297 K. MEM tests were conducted using guinea pig peritoneal macrophages mixed with supernatants from the lymphocytes to be tested. Reduction of MEM by the supernatant was considered a positive reaction to lymphokines released by the lymphocytes. Positive reactions were obtained with lymphocytes from 19 cancer patients and 15/93 controls and noncancer patients. Positive, results were obtained from 41/47 patients with colorectal cancer, 23/26 with gastric or esophageal cancer, 23/25 with otorhinolaryngological carcinoma, 5/7 with breast cancer, 11/12 with other cancers, and 2/2 with teratoma. Positive results were obtained from only 1/46 healthy controls but 14/47 patients without malignancies. Sensitivity to certain antigenic properties of teratomas evidently occurs in patients with cancers and also in patients with certain benign conditions. Whether this sensitivity is due to one antigen or to more than one is uncertain. (8 Refs)

OTHER RELATED STUDIES

49. NATURALLY OCCURRING ANTIBODIES AGAINST NINE COMMON ANTIGENS IN HUMANS SERA: II. HIGH INCIDENCE OF MONOCLONAL IG EXHIBITING ANTIBODY ACTIVITY AGAINST ACTIN AND TUBULIN AND SHARING ANTIBODY SPECIFICITIES WITH NATURAL ANTIBODIES.

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Unite d'immunocytochimie, Departement de Biologie Moleculaire, Institut Pasteur, 25, Rue du Docteur Roux, 75724 Paris Cedex 15, France
J Immunol; 128(6):2788-2792 1982

Previous results prompted us to check the sera of patients carrying either a multiple myeloma or a Waldenstrom's macroglobulinemia for the presence of monoclonal Ig (MIg) having antibody activity against tubulin, actin, thyroglobulin, myoglobin, fetuin, albumin, and transferrin. Among the 62 MIg studied against the seven above-mentioned antigens, 1 was shown to bind extensively to tubulin, and 4 bound mainly to actin, but a significant binding was also found to occur with tubulin and thyroglobulin. In all cases, findings were as follows: (1) The binding was mediated by light and heavy chain isotypes corresponding to those of the MIg. (2) The antibody function was located in the Fab fragments prepared by pepsin digestion of these MIg. (3) The antibody function was inhibited by the antigens. MIg with anti-tubulin activity was exclusively inhibited by tubulin, whereas the four MIg binding mainly to actin were predominantly inhibited by actin, but they were also strongly inhibited by tubulin and thyroglobulin. Similar results were obtained with either the serum or the F(ab')2 fragments. (4) The Fab fragments were tested for their capacity to stain, by immunocytologic procedures, cultured human hepatic cells previously treated with vinblastine. In the case of the serum exhibiting anti-tubulin activity, only paracrystals of tubulin were stained, whereas for the four MIg exhibiting anti-actin activity, simultaneous staining of actin filaments and tubulin paracrystals was observed. Three main conclusions emerge: (1) There is a high incidence of MIg possessing antibody activity directed against the cytoskeleton proteins. (2) These MIg seem to share antibody specificities with natural antibodies. (3) In the latter case, it can be postulated that, at least for some patients, the MIg may constitute the expansion of a clone producing a natural antibody. (14 Refs)

50. IDENTIFICATION OF IMMUNOGLOBULIN CLASS AND SUBCLASS OF MOUSE MONOCLONAL ANTIBODIES TO HUMAN CELL SURFACE ANTIGENS BY MIXED HEMADSORPTION ASSAY.

Liao SK, Kwong PC, Dent PB, Clarke BJ
Dept. Pathology, McMasters Univ. Health Sciences Centre, Room 4H2, Main St. West, Hamilton, Ontario L8N 3Z5, Canada
J Immunoassay; 2(3/4):227-238 1981

An assay modified from the conventional mixed hemadsorption technique to determine immunoglobulin (Ig) class or Ig subclass using minute amounts of unconcentrated culture supernatants of the hybridomas is described. Seven mouse monoclonal antibodies and the human melanoma cell line CaCL 78-1 were used. Results indicated that monoclonal antibody 87.20 belonged to IgG1; 140.96, IgG1; 7.51, IgG1; 7.60, IgG2a; 140.72, IgG1; 140.240, IgG2a; and 214.1AP1, IgM. Only the mouse IgG subclass corresponding to the specificity of the previously determined most reactive rabbit subclass antiserum efficiently eliminated the reactivity of that serum. (17 Refs)

51. EXPRESSION OF EUKARYOTIC VIRAL AND CELLULAR GENES.

Pettersson RF, Kaariainen L, Soderlund H, Oker-Blom N
Dept. Virology, Univ. Helsinki, Helsinki, Finland
Expression of Eukaryotic Viral and Cellular Genes. London, Academic Press, 324 pp., 1981.

Recent advances in molecular virology, molecular genetics, and recombinant DNA research are combined in a discussion of expression of eukaryotic viral and cellular genes. Structure and expression of DNA virus genes are reviewed with respect to molecular analysis of adenovirus transformation, control of adenovirus messenger (m)RNA production by differential transcription and differential stability of mRNA, an early adenovirus glycoprotein and its association with transplantation antigens, the control of adenovirus early gene expression, and mutational analysis of regulatory elements of simian virus 40. Retrovirus genes are discussed with respect to OK 10 virus-transformed bone-marrow-derived cell line, the transforming insert in the Abelson murine leukemia virus genome, and DNA intermediates in the replication of retroviruses. RNA virus genes are discussed with respect to the genome of single-stranded messenger-sense RNA viruses, influenza virus, capped cellular RNAs, drift and shift of influenza A-type virus, vesicular stomatitis virus and host cell phosphoproteins, initiation of eukaryotic protein synthesis, alphavirus gene products, Semliki Forest virus, RNA containing heterogeneous 5'-terminal nucleotide sequences, and Semliki Forest virus defective interfering RNA using DNA copies. Eukaryotic genes are discussed with respect to structure, organization and developmental expression of chorion multigene families, gene amplification and methotrexate resistance, RNA-protein complexes precipitated by Lupus antibodies, promoter sequences, expression of cloned eukaryotic genes in microorganisms, human genomic DNA-encoding Pro-opiomelanocortin, and functional yeast minichromosomes containing centromeric DNA. (701 Refs)

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IMMUNOBIOLOGY AND CANCER

Tumor-Associated Antigens

SERIES CB05 No. 82/12

DECEMBER, 1982

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DETECTION/ CHARACTERIZATION/ ISOLATION

1. A NEW MARKER FOR HUMAN CANCER CELLS. 1. THE CA ANTIGEN AND THE CA1 ANTIBODY.

Ashall F, Bramwell ME, Harris H
(c/o Harris) Sir William Dunn Sch. Pathology, Univ. Oxford, South Parks Road, Oxford OX1 3RE, England
Lancet; 2(8288):1-6 1982

In a search for antibodies that might distinguish between malignant and non-malignant cells a panel of matched pairs of hybrid cells produced by fusion of diploid fibroblasts with malignant cells originating from a cervical carcinoma was used as a screen. Each pair consisted of a hybrid in which malignancy was suppressed and a malignant segregant derived from this hybrid. A monoclonal antibody, designated Ca1, was found that discriminated absolutely between the hybrids in which malignancy was suppressed and the malignant segregants. This antibody detected an antigen present in the cell membranes of a wide variety of malignant human cell lines but not of diploid human cell strains. The antigen was found in very low concentrations, if at all, in homogenates of normal adult or fetal tis-

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sues. It could be immunoprecipitated by the Ca1 antibody from extracts of malignant cells but not from extracts of non-malignant cells. After reduction, the immunoprecipitated antigen separated in sodium dodecyl sulfate acrylamide gels as two bands with approx molecular masses of 390,000 and 350,000. These two components had the properties of glycoproteins with a high carbohydrate content; both bound the Ca1 antibody. The antigenic determinant resisted boiling at 100 C and extraction by a range of organic solvents. The binding of the Ca1 antibody to the antigen was substantially reduced by treatment of the antigen with neuraminidase, and the antigenic determinant was largely destroyed by certain endoglycosidases and by extensive proteolysis. Pending its further characterization, this antigen has been called the Ca antigen. (Author abstract) (24 Refs)

2. A NEW MARKER FOR HUMAN CANCER CELLS. 2. IMMUNOHISTOCHEMICAL DETECTION OF THE CA ANTIGEN IN HUMAN TISSUES WITH THE CA1 ANTIBODY.

McGee JO, Woods JC, Ashall F, Bramwell ME, Harris H
Nuffield Dept. Pathology, Univ. Oxford, John Radcliffe Hosp., Oxford OX2 9DU, England
Lancet; 2(8288):7-10 1982

The Ca1 antibody has been used in an immunohistochemical procedure to detect the Ca antigen in sections of tissues routinely embedded in paraffin wax. A representative sample of benign and malignant tumors from all the systems of the human body has been examined. The majority of malignant tumors express the Ca antigen. The exceptions are: prostatic carcinomas, testicular teratocarcinomas and seminomas, some sarcomas, some lymphomas, malignant brain tumors, neuroblastomas, and melanomas. The antigen is least readily detected in epithelial malignancies of the alimentary system, particularly the colon. The Ca1 antibody does not react with any benign tumor. The only normal tissues that react specifically with this antibody are the epithelium of the fallopian tube and the transitional epithelium of the urinary tract. The Ca1 antibody also readily distinguishes malignant cells in smears of malignant effusions. These findings indicate that the Ca1 antibody may be useful in the diagnosis of malignancy in routine clinical practice where the morphological interpretation of the biopsy or cytological smear is in doubt. (Author abstract) (2 Refs)

3. UNIQUE CELL SURFACE GLYCOPROTEIN EXPRESSION IN HAIRY CELL LEUKEMIA: EFFECT OF PHORBOL ESTER TUMOR PROMOTERS ON SURFACE GLYCOPROTEINS, CELL MORPHOLOGY, AND ADHERENCE.

Lockney MW, Golomb HM, Dawson G
(c/o Dawson) Dept. Pediatrics, Joseph P. Kennedy Jr. Mental Retardation Res. Center, Pritzker Sch. Medicine, Univ. Chicago, Chicago, IL, 60637
Cancer Res; 42(9):3724-3728 1982

Hairy cell leukemia cells from eight different patients exhibited a characteristic cell surface glycoprotein pattern when labeled by the neuraminidase-galactose oxidase-NaB3H4 procedure. The diffuse high-mol-wt glycoprotein band (Mr 230,000 to 300,000) was not seen in other leukemic cell types and may represent a specific hairy cell leukemia antigen. Hairy cell leukemia cells can be maintained as cell suspension cultures, but treatment with a variety of tumor-promoting phorbol esters caused the cells to adhere to plates, assume a fibroblastic elongated shape, and extend long processes. This dramatic morphological change was not associated with any change in surface glycoproteins. (Author abstract) (20 Refs)

4. HETEROGENEITY OF HUMAN MELANOMA-ASSOCIATED ANTIGENS DEFINED BY MONOCLONAL ANTIBODIES AND CONVENTIONAL XENOANTISERA.

Wilson BS, Kay NE, Imai K, Ferrone S
(c/o Ferrone) Dept. Pathology and Surgery, Coll. Physicians and Surgeons, Columbia Univ., 630 W. 168th St., New York, NY, 10032
Cancer Immunol Immunother; 13(1):69-74 1982

Types of 94,000 (94K) dalton and high-mol-wt antigens synthesized by cultured melanoma cells were studied. The monoclonal antibodies (MoAb) 376.96S, and 465.12S, and the polyclonal xenoantisera 8823 and 8986 all immunoprecipitated structures which when electrophoresed under reducing conditions gave apparent molecular weights of 94K. Sodium dodecyl sulfate polyacrylamide gel electrophoresis under nonreducing conditions showed that the 94K dalton molecules detected by the xenoantiserum 8823 exhibited a decrease in apparent mol wt to 82K daltons, while the structures identified by MoAb 465.12S, 376.96S, and xenoantiserum 8986 showed a decrease in apparent mol wt to 86K daltons. The MoAb 376.96S occasionally detected a small amount of 94K component in the spent medium of cultured melanoma cells, the xenoantiserum 8823 reacted with fibronectin while the MoAb 465.12 and xenoantiserum 8986 immunoprecipitated a major 94K and a minor 72K dalton structure. Immunodepletion experiments showed that the MoAb 465.12 and the xenoantiserum 8986 each reacts with the same population of 94K dalton molecules present in the spent medium of 3H-glucosamine-labeled melanoma cells. MoAb 225.28S and the xenoantiserum 8995 both immunoprecipitated two components from 3H-glucosamine-labeled melanoma cells BwV. Data indicated that the antigenic determinant detected by the MoAb 225.28S is not present on all the molecules comprising the 280K and greater than 440K dalton high-mol-wt melanoma-associated antigen system. (24 Refs)

5. LOCALIZATION OF S-100 PROTEIN AND GLIAL FIBRILLARY ACIDIC PROTEIN-RELATED ANTIGEN IN PLEOMORPHIC ADENOMA OF THE SALIVARY GLANDS.

Nakazato Y, Ishizeki J, Takahashi K, Yamaguchi H, Kamei T, Mori T
Dept. Pathology, Gunma Univ. Sch. Medicine, Showa-machi 3-39-22, Maebashi-shi, Gunma-ken 371, Japan
Lab Invest; 46(6):621-626 1982

Pleomorphic adenoma of the salivary glands was studied by the peroxidase-antiperoxidase method and Ouchterlony's double diffusion for the presence of so-called nervous system-specific proteins, S-100 protein, glial fibrillary acidic protein (GFAP), and astroprotein. Positive immunostaining for S-100 protein was observed in tumor cells of epithelial, myxomatous, and chondroid areas. An immunodiffusion test confirmed its presence in the tumor. Normal salivary glands were also stained with anti-S-100 serum, but the reaction was less intense than that of tumor. Specific immunostaining for GFSAP and astroprotein was found in a small number of cells of myxomatous and chondroid areas and occasionally in cells in epithelial areas. An immunodiffusion test suggests that the GFAP-related antigen of the pleomorphic adenoma showing a minor heterogeneity of antigenic determinants is almost identical with GFAP. Normal salivary glands did not stain with GFAP or astroprotein antisera, nor did they react with anti-GFAP serum by immunodiffusion. Thus, the S-100 protein and GFAP-related antigen may be actively synthesized in adenoma cells during the course of tumor development. In addition, the GFAP-related antigen is considered to be a tumor-associated antigen of pleomorphic adenoma of the salivary glands. (Author abstract) (28 Refs)

6. MONOCLONAL ANTIBODIES TO A HUMAN PROSTATE ANTIGEN.

Frankel AE, Rouse RV, Wang MC, Chu TM, Herzenberg LA
Cetus Immune Corporation, 3400 West Bayshore Drive, Palo Alto, CA, 94305
Cancer Res; 42(9):3714-3718 1982

Three monoclonal antibodies reactive with a purified extractable Mr 34,000 prostate antigen (PA) have been prepared by fusing splenocytes of BALB/c mice preimmunized with purified PA with the NS1 mouse myeloma cell line. The three antibodies were all of the IgG-1 subclass. The antibodies defined two noncross-blocking unique determinants on PA; each present as one site per molecule. IF3 defined on antigenic site and 2G7 and 1C5 defined another antigenic determinant. All of the antibodies reacted with PA in a solid-phase radioimmunoassay and immunoprecipitated 125I-labeled PA. Absorption and sandwich radioimmunoassays showed PA in prostate tissues but not in tonsil, liver, or kidney. Immunoperoxidase staining of formalin-fixed paraffin-embedded sections of benign prostatic hyperplasia and prostatic carcinoma revealed strong prostate epithelial reactivity. None of the antibodies showed reactivity with prostate membrane preparations. A sandwich radioimmunoassay used 2G7 as a plate coat. 125I-labeled 1F3 was used to detect 5 ng PA per ml in sera of patients with prostate cancer. These results confirm previous observations regarding the specificity of PA and shed new evidence for its intracellular localization. (Author abstract) (17 Refs)

7. IMMUNOCHEMICAL DEMONSTRATION OF AN OVARIAN CANCER-ASSOCIATED URINARY PEPTIDE.

Stenman UH, Huhtala ML, Koistinen R, Seppala M
I, II Dept. Obstetrics and Gynecology, Helsinki Univ. Central Hosp., SF-00290 Helsinki 29, Finland
Int J Cancer; 30(1):53-57 1982

Immunization with a peptide fraction from ovarian cancer urine resulted in an antiserum that reacts with a 6,000-dalton (6K) peptide. In urine from some patients with advanced gynecological cancer, the concentration of 6K peptide was high enough to be detected by immunodiffusion. By radioimmunoassay the levels in normal serum could be determined. The concentration in serum was 5-20 ug/l and that in urine 5-50 ug/l. Elevated levels were observed in urine from 5 out of 8 patients with ovarian cancer, 10 out of 14 patients with cervical cancer and 9 out of 14 patients with endometrial cancer. The highest level observed was 12,000 ug/l. High concentrations of the 6K peptide (100-300 ug/l) were observed in amniotic fluid from 14-16 weeks of pregnancy. Some tumor extracts also had a high concentration of the 6K peptide. No immunological relationship was observed between the peptide and known tumor-associated antigens or serum proteins. These results suggest that the peptide is a new oncodevelopmental peptide which may have significance as a tumor marker. (Author abstract) (17 Refs)

8. EXPRESSION ON CULTURED HUMAN TUMOUR CELLS OF PLACENTAL TROPHOBLAST MEMBRANE ANTIGENS AND PLACENTAL ALKALINE PHOSPHATASE DEFINED BY MONOCLONAL ANTIBODIES.

McLaughlin PJ, Cheng MH, Slade MB, Johnson PM
Dept. Immunology, Univ. Liverpool, P. O. Box 147, Liverpool L69 3BX, England
Int J Cancer; 30(1):21-26 1982

The cellular reactivity of six monoclonal antibodies (McAbs) produced to isolated human placental syncytiotrophoblast microvillous plasma membranes has been examined using a variety of normal and malignant cell types. Two McAbs reacted with antigenic determinants common to most normal human cells. Two other McAbs (H310 and H316) reacted predominantly with normal placental trophoblast and with lymphocytic cells, as well as with most transformed or neoplastic cultured cell lines. Two further McAbs (H315 and H317) identified fetal differentiation antigens expressed only on the membranes of normal placental trophoblast and of certain tumor cell lines. H317 has been shown to be specific for the heat-stable L-phenylalanine-inhibitable placental-type alkaline phosphatase isoenzyme. These latter McAbs (H315 and H317) may prove useful in monitoring of some human cancers. (Author abstract) (36 Refs)

9. QUANTITATION OF A 55K CELLULAR PROTEIN: SIMILAR AMOUNT AND INSTABILILTY IN NORMAL AND MALIGNANT MOUSE CELL LINES.

Mora PT, Chandrasekaran K, Hoffman JC, McFarland VW
Macromolecular Biology Section, NCI, NIH, Bethesda, MD, 20205
Mol Cell Biol; 2(7):763-771 1982

Quantitative expression of a specific 55,000 mol wt (55K) cell protein was studied in two groups of mouse fibroblast (clonal) cells from two parental clones, one with high (HT), the other with low tumorigenicity (LT). From the LT clone, tumor lines and clones were obtained by selecting rare, spontaneously transformed highly tumorigenic (mutant) cells. Cells were labeled during exponential growth with 35S-methionine, and the 55K protein was immunoprecipitated with a monoclonal antibody and quantitated. There were low and approx equal amounts of 55K in cells (clones) with both low and high tumorigenicity from both groups of cells; there was no correlation between quantitative expression of 55K protein and cellular tumorigenicity. As shown previously, there was approx 10 to 20-fold more 55K protein in all simian virus 40 (SV40)-transformed T antigen-positive derivative clones. The T antigen-negative revertant tumor lines and clones obtained by an immunological in vivo selection method had low amounts of 55K protein, as in the parent cell before SV40 transformation. In all T antigen negative cells (including highly tumorigenic cells), degradation of the 55K protein was rapid, with a half-life of 15-60 min. The 55K protein was stable in all T antigen-positive cells (half-life greater than 10 hr). There was a very low, or an undetectable amount of the 55K protein in primary cells established from the tumors induced by highly tumorigenic cells. In contrast, primary cells obtained from early murine embryos had large amounts of (stable) 55K proteins. (30 Refs)

10. NONCYTOLYTIC EXTRACTION OF MURINE TUMOR-SPECIFIC TRANSPLANTATION ANTIGENS WITH THE NONIONIC DETERGENT OCTYL-BETA-D-GLUCOPYRANOSIDE.

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JNCI; 69(1):131-136 1982

The nonionic detergent octyl-beta-D-glucopyranoside (C3Glu) was used to extract immunogenic tumor-specific transplantation antigen (TSTA) from intact cells and purified plasma membranes of the 3-methylcholanthrene-induced fibrosarcoma MCA-F. Pretreatment of syngeneic C3H/HeJ mice with 100 ug of C8Glu extracts induced specific immunoprotection such that mice resisted the outgrowth of MCA-F but not the antigenically distinct tumors MCA-D or MCA-2A. Incubation of intact cells with 7 mM (0.2%) C8Glu for 30 minutes at 23 C was judged to be noncytolytic because extracted cells excluded trypan blue. Preparative isoelectric focusing partially purified the MCA-F-specific antigen from crude C8Glu extracts into the pH 6.5-6.8 region of the gradient. Electrofocusing yielded 60% of the applied antigen activity and a fourfold to fivefold increase in specific activity. In addition, immunoprospective activity was obtained in 2% C8Glu extract of MCA-F plasma membranes, confirming the membrane localization of the MCA-F TSTA. Three properties of C8Glu rendered it an attractive agent for the preparation of cell surface proteins: a nonionic character, large critical micellar concentration, and its capacity to extract antigens without complete membrane solubilization or cell disruption. (Author abstract) (30 Refs)

11. NEUTRAL GLYCOLIPID ANTIGENS AS DEVELOPMENTAL MARKERS OF MOUSE TERATOCARCINOMA AND EARLY EMBRYOS: AN IMMUNOLOGIC AND CHEMICAL ANALYSIS.

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J Immunol; 129(2):603-609 1982

Purified rabbit antibodies to neural glycolipids were analyzed for their binding to mouse embryonal carcinoma cells (ECC) and preimplantation mouse embryos. Antibodies to globotetraosylceramide first bind to two to four-cell embryos and reach a peak of staining intensity with morulae, whereas anti-Forssman antibodies first bind to late morulae and then, most intensely, to early blastocysts. We compared the binding of a monoclonal anti-Forssman antibody with that of rabbit anti-Forssman antibodies and show that although they react similarly with ECC, they do not do so with morulae: the monoclonal antibody stained weakly and unevenly, whereas the rabbit antiserum produced a uniformly bright immunofluorescent staining. Chemical analyses revealed that globotetraosylceramide is the most abundant glycolipid of F9 ECC and that there is poor correlation between the concentration of individual glycolipids in these cells and their reactivity with antibodies to glycolipid molecules. Interestingly, the two Forssman antibody-reactive glycolipids of F9 ECC differ in their mobility on TLC plates from the classical Forssman antigen extracted from sheep red blood cells. This illustrates the potential problems in extrapolating from the coincident binding properties of an anti-glycolipid antibody to the chemical structure or abundance of an antigen in different cell types. (Author abstract) (45 Refs)

IMMUNOLOGICAL STUDIES

12. ISOLATION OF MYELOID PROGENITOR CELLS FROM PERIPHERAL BLOOD OF CHRONIC MYELOGENOUS LEUKEMIA PATIENTS.

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Blood; 60(1):30-37 1982

Myeloid progenitor cells (colony- and cluster-forming cells in semisolid medium, CFU-GM) were purified from the peripheral blood of chronic myelogenous leukemia (CML) patients. Lymphocytes, monocytes, and most immature myeloid cells were simultaneously depleted with specific monoclonal antibodies using an erythrocyte rosette technique for cell separation. Cells expressing Ia-like antigen were then selected from the residual cell population. Day 7 CFU-GM were enriched 44-116-fold in the Ia+ cell fraction, when compared to the unseparated cells, and up to 47% of the cells could form a myeloid colony or cluster in culture. This cell fraction contained up to 92% undifferentiated blasts, with the remainder mostly promyelocytes. The enriched CFU-GM cells were dependent on an exogenous supply of colony-stimulating factor for growth, and colony formation was linear with cell concentration over a large range (10(4) -10(1) cells/ml). This technique of rosette depletion and enrichment with specific monoclonal antibodies provides a unique method for purifying a homogenous population of myeloid precursor cells with defined surface antigen characteristics. (Author abstract) (50 Refs)

13. PROBING HUMAN MALIGNANT T CELLS WITH LECTINS: A COMPARISON WITH THEIR SURFACE ANTIGEN PATTERNS DEFINED BY MONOCLONAL ANTIBODIES.

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Leuk Res; 6(3):307-312 1982

Tumor populations (TP) of 53 patients (40 children, 13 adults) with T cell malignancies were investigated with lectins and the lectin- and monoclonal antibodies-defined phenotypes were compared. Fifteen patients had TP resembling early thymocytes (T6-, T3-phenotype): 2 had peanut agglutinin positive (PNA+) and soybean agglutinin positive (SBA+) malignant cells (1 child with lymphoblastic lymphoma, 1 adult with acute lymphoblastic leukemia), and 13 had PNA-negative (PNA-) and SBA-negative (SBA-) malignant cells. Among the patients with T6+, T3-tumor cell populations resembling corticothymocytes (15 children, 1 adult), five had PNA-, SBA- malignant T cells; three PNA+, SBA+; seven PNA+, SBA-; and one PNA-, SBA+ malignant T cells. Six patients (5 children, 1 adult) had cells displaying both T6 and T3 antigens. Three of the six patients had PNA+, SBA- cells; two PNA-, SBA+; and one PNA-, SBA- cells. Among 16 patients (6 children, 10 adults) with T6-, T3+ malignant cells, 13 had PNA-, SBA- cells, thus resembling peripheral T cells. Three of 16 patient with T6-, T3+ cells had PNA-, SBA+ cells. These cell populations can be related to medullary thymocytes rather than peripheral T cells. The results showed that in spite of a high degree of heterogeneity of malignant T cell populations in the pattern of surface antigens, the populations appear to conform essentially to the scheme of normal T cell differentiation. (28 Refs)

14. A PHORBOL ESTER TUMOR PROMOTER INDUCES CHANGES IN THE EXPRESSION OF IMMUNOGLOBULINS AND DR ANTIGENS IN HUMAN LYMPHOBLASTOID CELLS.

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J Immunol; 129(2):539-544 1982

The present study indicates that 12-O-tetradecanoyl phorbol 13-acetate (TPA) can induce either increases or decreases in the relative expression of membrane-associated IgM and IgD as well as the expression of other markers of lymphocyte differentiation on human B lymphoblasts, depending on the clone studied. The changes in membrane Ig expression are apparent within 24 hr and are maximal at about 48 hr after the addition of the compound. In clone BL, TPA decreases the membrane IgM/IgD ratio as determined by the percentage of cells bearing these isotypes and by their densities on single cells. In clone MW-E, TPA has the opposite effect. Although these changes are followed by an increase in Ig secretion by MW-E cells, measured by immunofluorescence and the protein A plaque assay, There is no induction of Ig secretion in BL cells. In addition, TPA increases the expression in BL of an additional B lymphocyte marker, the D region-related (DR) antigens, while having the opposite effect in MW-E. In two sublines of Daudi, a membrane IgM-positive, IgD-negative, nonsecreting cell line, TPA treatment resulted in the expression of membrane IgD without the induction of Ig secretion. Thus, the TPA-induced changes in the IgM/IgD ratio and Dr antigen expression are inversely related and are not due to differential proliferation of subpopulations. Taken together, it appears that, depending on the particular clone of B lymphoblasts studied, TPA can induce or inhibit a coherent program of B lymphocyte maturation. (Author abstract) (52 Refs)

15. ANTIGENS OF THE BASEMENT MEMBRANE AND THE PERITUMORAL STROMA IN HUMAN COLONIC ADENOCARCINOMAS: AN IMMUNOFLUORESCENCE STUDY.

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Int J Cancer; 30(1):13-20 1982

Twenty colonic adenocarcinomas were studied by immunofluorescence with antisera against components of the basement membrane: Type IV collagen, laminin and heparan sulfate-rich proteoglycan, as well as antisera against antigens of the connective tissue: Type-III collagen, fibronectin and hyaluronectin. Marked alterations of the basement membranes were consistently observed on staining with each one of the first three antisera. In contrast, staining of the normal components of connective tissue was in most cases as intense as in normal colonic mucosa. Hyaluronectin, a marker of peritumoral stroma, was found to be present in 12 out of 15 tumors studied. (Author abstract) (22 Refs)

16. EXPRESSION OF NEUROECTODERMAL ANTIGENS COMMON TO MELANOMAS, GLIOMAS, AND NEUROBLASTOMAS. I. IDENTIFICATION BY MONOCLONAL ANTI-MELANOMA AND ANTI-GLIOMA ANTIBODIES.

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Acta Neuropathol (Berl); 57(2/3):158-164 1982

In studies in mice, the reactivity spectrum of five monoclonal anti-melanoma antibodies (Ab; Mel-5, Mel-14, Me3-TB7, Me4-F8, Me5-D5) cross-reacting with gliomas and neuroblastomas and one monoclonal anti-glioma Ab was determined in an Ab-binding radioimmunoassay. Ab from Me5 bound to 5/7 gliomas and to 3/3 neuroblastomas. Ab from Mel-14 also bound to 5/7 gliomas but to only one neuroblastoma. Similar, but not identical cross-reactivities, occurred with the other anti-melanoma clones. None of the anti-melanoma clones reacted with 33 non-melanoma control cell lines. The monoclonal anti-glioma Ab, G13-C6, bound to 8/9 melanoma cell lines and to 1/3 neuroblastoma lines. Results of the study indicated that the antigenic determinants detected by these Ab were not associated with the same antigen, thus suggesting the existence of at least six different antigens common to melanomas, gliomas, and neuroblastomas. While all the tumors studied are derived embryologically from the neural crest, absorption with homogenate of a whole brain of a fetus at 20 wk of gestation abolished only the binding of monoclonal anti-glioma antibody, but did not modify the binding of monoclonal anti-melanoma Ab. (16 Refs)

17. THE ANTIGENICITY OF ELECTROCAUTERIZED ALLOGENEIC TUMOR CELLS IN MICE.

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J Surg Res; 33(1):17-22 1982

This study was conducted in order to establish the effects of electrocautery on the immunogenicity of allogeneic tumor cells as measured by cellular and humorally mediated responses. Balb/c mice were immunized with either cauterized or noncauterized EL4 tumor cells from C57Bl/6J mice. At 7 and 13 days postimmunization, humoral (CDC) and cell-mediated (CMC) responses were tested. Animals receiving cauterized or noncauterized EL4 cells had specific and significantly greater (p less than 0.001) CDC and CMC at 13 days than did nonimmunized animals. This study demonstrates that electrothermal destruction of allogeneic tumor cells does not prevent antigenic recognition by recipients. This might be clinically relevant if electrocoagulation is used to eradicate rectal and other carcinomas and yet allow immune recognition of tumor antigens should they exist. (Author abstract) (5 Refs)

18. CELL SURFACE ANTIGEN PHENOTYPES AND ENZYME EXPRESSION PATTERNS OF TWO MURINE T-CELL LYMPHOMAS DERIVED FROM EARLY AND/OR MATURE THYMUS CELLS.

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Leuk Res; 6(3):425-428 1982

Expression of cell surface antigens on SL2 and GRSL13 cells and enzyme cytochemistry of murine SL2 and GRSL13 lymphoma cells were investigated. SL2 lymphoma occurred as a spontaneous tumor in DBA/2 mice, and GRSL13 lymphoma occurred as a spontaneous lymphoma in GRS mice. While T200 antigen expression was high on both lymphomas, Thy1 was low on GRSL13 and high on SL2. Significant difference between the two lymphomas was obtained using antibodies 30-G12 (anti-T200) and 30-H11 (anti-glycolipid) with positivity on GRSL13 and no reaction on SL2; a reverse pattern was seen with antibodies 53-7.3 (anti-Lyt1) and 53-6.7 (anti-Lyt2). Since ThB and the glycolipid detected by antibody 30-H11 were expressed on bone marrow cells and since ThB was not expressed at all on peripheral T cells, the antigens are apparently characteristic for the more primitive cells in the thymic series. Results showed that GRSL13 represents a T cell of a more primitive immature type, while SL2 represents a more mature T cell. Enzymes present and clearly expressed in the lymphomas as well as the majority of thymus cells were acid phosphatase, beta-glucuronidase, non-specific esterase, and alphanaphthyl-acetate-esterase. No clear difference was observed between the two lymphomas and the normal thymus cells. (17 Refs)

19. ISOLATION AND CHARACTERIZATION OF PEANUT AGGLUTININ-RESISTANT EMBRYONAL CARCINOMA CELL-SURFACE VARIANTS.

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J Cell Physiol; 112(2):162-170 1982

Isolation and characterization of embryonal carcinoma cell lines resistant to the cytotoxic effect of peanut agglutinin (PNA) is described. Parental cells were the pluripotent embryonal carcinoma cell lines PSA-1 and a hypoxanthine phosphoribosyltransferase-deficient, ouabain-resistant subclone, OPST-42. PNA-resistant clones were isolated at a frequency of 4 x 10(-5) following mutagenesis. All eight clones tested remained resistant to PNA after growth in nonselective medium. Somatic cell hybrids between PNA-resistant cells and PNA-sensitive cells suggested that the PNA-resistance in the mutants was recessive. Binding assays demonstrated that resistant cells exhibited a two- to four-fold reduction in the total amount of PNA bound, compared with parental lines. All eight PNA-resistant cell lines formed well-differentiated teratocarcinomas in syngeneic mice and the tumors contained cells resistant to PNA. When incubated in suspension with endodermal cells, the PNA-resistant cells sorted out to form simple embryoid bodies. The PNA-resistant cells showed reduced expression of stage-specific embryonic antigen 1. Thus, embryonal carcinoma cells can form tumors, differentiate, and recognize differentiated cells in a sorting assay, even though they have a reduction in expression of the embryo-specific cell surface structures that bind PNA and anti-stage-specific embryonic antigen-1 antibody. (42 Refs)

20. NATURALLY OCCURRING ANTIBODIES AGAINST FIBROSARCOMA AND GLIOMA CELLS IN RATS.

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Gan; 73(3):454-461 1982

The presence of natural antibodies (NA) against fibrosarcoma and glioma cells was detected in the normal sera of 10 different strains of rats. By means of a complement-dependent cytotoxicity test and an absorption test, the NA-reactive antigens were detected in all investigated syngeneic and allogeneic fibrosarcoma lines and one glioma line, but not in hepatoma, lymphoma, leukemia, and neurinoma lines. Moreover, the cytotoxic activity of NA was significantly absorbed by normal brain, lung, kidney, skin homogenates, and cultured fibroblasts of syngeneic rats, but not by liver homogenates, thymus, spleen, lymph node or red blood cells. With the exception of a Donryu rat strain, there were no strain or sex differences in the NA levels among the investigated strains of rats. The NA were biochemically identified as being IgM and were stable at 56 C for 30 min. The level of NA correlated with the in vivo antitumor response: when NA-reactive fibrosarcoma or glioma cells were implanted into syngeneic WKA/Hok rats, groups of rats with high NA levels showed suppression of tumor growth and prolongation of survival time as compared to groups of rats with low NA levels, while there was no difference in survival time of rats transplanted with NA non-reactive hepatoma or lymphoma lines. When 3-methylcholanthrene was inoculated into rats, the tumor incidence in the group of rats with high NA levels was significantly suppressed as compared to the group of rats with low NA levels. (Author abstract) (18 Refs)

21. PRODUCTION OF A TUMOR-SPECIFIC XENOANTISERUM FROM PARTIALLY PURIFIED IMMUNOPROTECTIVE TUMOR ANTIGEN.

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Cancer Immunol Immunother; 13(1):48-52 1982

Raising of specific xenoantisera in rabbits by purified tumor-specific transplantation antigens (TSTA) preparations was studied. Serum from the rabbit immunized with partially purified 3-methylcholanthrene (MCA)-F tumor TSTA (fraction 15, Fr 15) displayed a complete or semi-circular ring reaction in the immunofluorescence assay at a titer of 1:4 when a fluorescein isothiocyanate-conjugated goat anti-rabbit IgG serum was used at a dilution of 1:8. Absorption with 10(8) intact MCA-F cells diminished the ability of 1 ml anti-Fr 15 serum to bind MCA-F cells by 95%. On the other hand, absorption with MCA-D or MCA-T cells did not significantly inhibit the immunofluorescence reaction. Preincubation with 30 mg 3 M KCl extract or with 7.5 mg Fr 15 completely inhibited the binding capacity of 1 ml anti-Fr 15 serum. No significant difference in the fluorescence between cells stained after 5-hr incubation at 37 C and cells stained immediately was observed. Thus neither macrophages nor other Fc receptor-bearing cells significantly contributed to the proportion of tumor-derived cells exhibiting fluorescence. The xenoantibody displayed specific immunologic reactivity in the indirect membrane immunofluorescence assay, suggesting that administration of purified materials may afford new reagents with which to dissect and purify TSTA. (23 Refs)

VIRUS ASSOCIATED ANTIGENS

22. EXPRESSION OF HERPES SIMPLEX VIRUS TYPE 2 ANTIGENS IN PREMALIGNANT AND MALIGNANT HUMAN VULVAR CELLS.

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Am J Obstet Gynecol; 143(6):611-619 1982

Vulvar biopsies and explants from patients with vulvitis, hyperkeratosis, condyloma acuminatum, severe dysplasia, and squamous cell carcinoma were screened for herpes simplex virus Type 2 (HSV-2) antigens. Immunoperoxidase staining for VP143, an early nonstructural polypeptide of HSV-2, was identified within three biopsies exhibiting severe dysplasia, three of seven with carcinoma in situ, and one of three with invasive squamous cell carcinoma. Similar staining for VP143 was observed in derived explants. Staining for VP119, the major envelope glycoproteins of HSV-2, was identified within tissues which were positive for VP143. Both proteins were expressed in the absence of staining for virus capsid proteins, detection of virus structures by electron microscopy, and isolation of infectious virus by co-cultivation, indicating that only a fragment of the virus genome was expressed. Neither VP143 nor VP119 was identified in biopsies exhibiting vulvitis, hyperkeratosis, or condyloma acuminatum. These data indicate a close relationship between HSV-2 and vulvar neoplasia. (Author abstract) (19 Refs)

23. PERSISTENT ACTIVE INFECTION OF EPSTEIN-BARR VIRUS (EBV) IN CARRIER FEMALES OF THE X-LINKED LYMPHOPROLIFERATIVE SYNDROME (XLP).

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Excerpta Med Int Congr Ser; 571:375-379 1982

Among conditions that may follow infection with Epstein-Barr virus (EBV), is malignant lymphoma in males affected by the X-linked lymphoproliferative syndrome (XLP). To test the hypothesis that the variable expression of XLP is manifested in obligate carrier females, blood from 12 obligate carrier females was studied for anti-viral capsid antigen (VCA), anti-early antigen (anti-EA) and anti-Epstein-Barr nuclear-associated antigen (EBNA). All carriers were seropositive to EBV. The reciprocal geometric mean titer for IgG anti-VCA was elevated to 570 in the carrier females compared to 100 in 24 controls. The range of anti-VCA was from 80 to 5,120. IgA class anti-VCA was found in 2/3 of the carriers. All but one of those with anti-VCA of IgA class showed anti-EA, indicative of active infection and immunodeficiency. About one-half of the carriers had persistent anti-EA antibodies. However, the anti-EBNA levels of carrier females were similar to those of the healthy controls. There was no apparent relationship between IgM level and EBV-specific antibody titers. The paradoxically elevated EBV-specific antibodies which tend to persist in obligate carriers of XLP provides an opportunity to define the immunopathology of XLP and to detect carrier females. (17 Refs)

24. IMMUNOCHEMICAL CHARACTERIZATION OF EBV ANTIGENS DETECTED BY DOUBLE IMMUNODIFFUSION.

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Dept. Tumor Biology, Karolinska Institutet, S-104 01 Stockholm, Sweden
Intervirology; 17(4):208-214 1982

Double immunodiffusion (Ouchterlony) tests gave regularly positive reactions when extracts of [35S]-methionine-labeled, n-butyrate-induced P3HR-1 cells were allowed to react with serum pools with high Epstein-Barr virus (EBV) antibody titers from Burkitt lymphoma or nasopharyngeal carcinoma patients, but not with EBV antibody-negative sera. Similarly prepared extracts of noninduced P3HR-1 cells gave no precipitation lines with the antibody-positive sera. The composition of the precipitates was analyzed by SDS-PAGE and compared with immunoprecipitates obtained by indirect immunoprecipitation in soln. Three lines precipitated on the Ouchterlony plate were analyzed; these lines were located at close (a), intermediate (b), and distant (c) positions in relation to the antigen well. Precipitate (a) contained polypeptides with mol wt of 165,000 (165K), 152K, 138K, 134K, 103K, and 55K. Precipitate (b) contained 152K and 138K as the major components, while 55K was relatively underrepresented. Precipitate (c) contained 90K and 55K as major components, while 152K was a minor component. The method is suitable for the study of possible subtype differences between defined antigenic components of the early and late EBV-determined antigen complexes. (Author abstract) (9 Refs)

25. SEROLOGIC TESTS FOR NASOPHARYNGEAL CARCINOMA IN NORTH AMERICAN PATIENTS.

Neel HB, Pearson GR, Weiland LH, Taylor WF
Mayo Clinic and Foundation, Rochester, MN
Excerpta Med Int Congr Ser; 582:111-114 1982

The clinical value of serum titers of various Epstein-Barr virus (EBV) related antibodies was investigated in 92 North American patients with primary nasopharyngeal carcinoma (NPC), 149 patients with head and neck cancer (HNC) other than nasopharyngeal, 342 patients with benign diseases (BD) commonly seen in large otolaryngologic practices, and 100 healthy blood donors. Antibody titers of sera from patients with untreated NPC differed significantly from those of the other groups. Positive titers for the IgA anti-viral capsid antigen were found in 70% of NPC patients, only 5% of those with HNC, and 10% of those with BD. Undifferentiated and nonkeratinizing carcinomas consistently exhibited elevated antibody titers directed against viral capsid antigen and early antigen. The incidence of elevated titers was lower in patients with keratinizing squamous cell carcinoma compared with the other groups. The incidence of positive IgA anti-viral capsid antigen titers in undifferentiated and nonkeratinizing varieties were much greater than those in keratinizing squamous cell varieties. A trend toward higher antibody titers with the development of metastases was seen. Of the 13 patients who died, 8 had low antibody-dependent cellular cytotoxicity titers at diagnosis and 4 had high titers. In general, patients with very high antibody-dependent cellular cytotoxicity titers remained free of disease for as long as 4 yr; these patients should be followed closely in order to determine the prognostic value of the EBV markers. (5 Refs)

26. HEPATITIS B VIRUS AND PRIMARY HEPATOCELLULAR CARCINOMA: FAMILY STUDIES IN KOREA.

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Int J Cancer; 30(1):47-51 1982

Chronic infection with hepatitis B virus (HBV) is closely associated with the etio-pathogenesis of primary hepatocellular carcinoma (PHC). It has been proposed that infection with HBV early in life, frequently transmitted by an HBV-carrier mother, leads to persistent infection with HBV, which in turn is associated with the development of chronic active hepatitis (CAH), post-necrotic cirrhosis and PHC. If this view is correct, then there should be clustering of chronic carriers of HBV in families of patients with chronic liver disease. We tested this hypothesis in Korea by collecting serum from 132 patients with these chronic liver diseases admitted to the Seoul National University Hospital and 664 of their first-degree relatives. Sera were assayed for hepatitis B surface antigen (HBsAg), antibody to HBsAg (anti-HBs) and antibody to hepatitis B core antigen (anti-HBc). Almost all cases showed evidence of present or past infection with HBV. Mothers of patients were more frequently HBsAg(+) than age-matched women in the control population or wives of patients. Five of 23 fathers were also HBsAg(+) compared with 1 of 25 age-matched controls. There was a deficit of anti-HBs in the fathers of cases compared with the controls. Siblings of patients were frequently HBsAg(+), with the highest prevalence in brothers. Family history shows that five fathers, two mothers and five brothers of cases have died of PHC. These data are compatible with the hypothesis tested and lend further support to the view that prevention of infection with HBV will lead to a marked decrease in the incidence of CAH, cirrhosis and PHC in areas where these diseases are endemic. Members of the families of patients with these diseases are at high risk of developing persistent infection with HBV and chronic liver disease. It would be appropriate to focus preventive strategies on infants and children in such families. (19 Refs)

27. ONCOVIRAL PROTEINS AS CELLULAR ANTIGENS.

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Curr Top Microbiol Immunol; 98:37-80 1982

The immunological recognition of proteins encoded by oncoviruses and the biological consequences of recognition are reviewed. Virally produced proteins include structural proteins of the virion, variants of these proteins that do not reside on the virions, and proteins that are coded by cellular genes that have become incorporated into the oncoviral genome. The last-mentioned type of protein can produce malignant transformation. Many viral proteins are found on the cell surface membrane and therefore act as antigens. As antigens, the proteins provide a target for immune response by the host. The immune response may be useful for in vitro serological analysis. The murine system has provided a model for study of immune response by the host to virion structural proteins and the expression of endogenous viral proteins in various hematopoietic cell lineages. The feline system has been a model for assessment of host responses to virally-induced malignancy. The feline system has produced the best evidence that an immune response by the host to viral transformation antigens can be decisive in rejection of a tumor and indicative of the incidence of a tumor in a population. Discussion emphasizes recognition in the host species from which particular viruses were derived. Only C-type viruses are discussed. (400 Refs)

28. THE PATHOGENESIS OF ABELSON VIRUS LYMPHOMAS OF THE MOUSE.

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Biochim Biophys Acta; 651(4):213-244 1982

The origin of the Abelson virus (AV) and the pathogenesis of the disease it induces are discussed. Before discussing Abelson murine leukemia virus (A-MuLV) in detail, some insights gained from the study of other RNA tumor viruses, both with respect to mechanisms of their action and host genetic responses to them, are presented. The main presentation comprises four sections. Virological and molecular characterization of AV involves its isolation, assays, genome structure of the helper and defective viruses, proteins encoded by the defective A-MuLV genome, and mutants of AV. Biology of AV diseases is discussed in relation to transformation of bone marrow cells by A-MuLV and pathogenesis. Differentiative phenotype of Abelson lymphomas and cell lines is discussed in relation to phenotypes of in vitro-derived lines, expression of lineage markers by tumors, and neoplastic differentiation of clonal Abelson lymphoma lines. With relation to cellular antigens identified on Abelson lymphoma and transformed cells, Abelson target-associated antigen, p50 and Abelson lymphoma antigens are discussed. A final section presents a summary of present knowledge, interpretations and further speculations on the involvement of AV in hematopoietic differentiation and neoplasia. (187 Refs)

29. SURFACE ANTIGEN EXPRESSED IN HEMATOPOIETIC CELLS DERIVED FROM FV-4 MOUSE STRAINS.

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Dept. Microbiology, Univ. Tokyo, P. O. Box Hongo, Tokyo 113, Japan
JNCI; 68(6):1005-1009 1982

Fv-4 locus controls the susceptibility of mice to ecotropic murine leukemia virus. Antiserum against Fv-4r/s mice with BALB/c background was raised in inbred BALB/c mice. In the complement-dependent cytotoxicity test, the antiserum killed the hematopoietic cells derived from Fv-4r/- mice but not those from Fv-4s/s mice, and the genetic cross experiments located the locus controlling the expression of the target molecule of the antibody in the close vicinity of Fv-4. In addition, the antigenic expression of the exogenously infecting MuLV suppressed the expression of the target molecule of the antiserum. The expressions of these two antigens appear to compete with each other on the cell surface. (Author abstract) (21 Refs)

30. ANTIGENIC AND CHROMOSOMAL CHANGES IN THYMUS AND SPLEEN OF BALB/MO MICE DURING LEUKEMOGENESIS.

Asjo B, Fenyo EM, Spira J
Dept. Tumor Biology, Karolinska Institutet, S 104 01 Stockholm, Sweden
Leuk Res; 6(3):413-419 1982

Correlation between the amplification of the Moloney murine leukemia virus (M-MuLV) and appearance of M-MuLV induced cell surface antigen, MCSA, on thymus cells was studied in Balb/Mo mice. Production of infectious virus in the preleukemic mice was accompanied by the appearance of viral p30 antigen on the surface of thymus cells. All organs of Balb/Mo mice were negative for MCSA up to 40 days. Thereafter occasional thymuses contained a low fraction of MCSA-positive cells. Thus, Balb/Mo mice differed from mice neonatally inoculated with M-MuLV since the amplification of the viral genome was not accompanied by the appearance of MCSA on thymus cells. Mice mainly developed lymphomas with two distinct clinical manifestations. One type was characterized primarily by enlargement of spleen and lymph nodes, and the other by enlargement of thymus with eventual infiltration of peripheral lymphatic organs. Leukemia latency varied between 3-10 mo and was not correlated with any particular type of lymphoma. Thymus cells were often MCSA positive while spleen cells of the same animal were MCSA negative. Based on the antigen patterns of thymomas and lymphomas, Balb/Mo lymphoma mice were more often negative for MCSA (68%) than mice receiving M-MuLV at birth (40%). The majority of thymus cells was MCSA positive while the spleen was MCSA negative. No correlation between the antigen expression and chromosome constitution could be observed. Amplification of the M-MuLV genome in young Balb/c mice was not accompanied by the appearance of MCSA on thymus cells. Results suggested that MCSA is related to a virus activated in a minority of Balb/Mo mice during the late phase of leukemogenesis. (14 Refs)

31. VIRUS INOCULATION IN MICE BEARING EHRLICH ASCITIC TUMORS: ANTIGEN PRODUCTION AND TUMOR REGRESSION.

Mettler NE, Clarke DH, Casals J
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Infect Immun; 37(1):23-27 1982

Ehrlich ascitic carcinoma, as developed in albino mice, has been used as a source of hemagglutinating and complement-fixing antigens, and it proved to be suitable for one type of antigen, or both, for at least 12 viruses of 16 tested. Hemagglutinins were obtained with members of arbovirus groups A, B, and C; complement-fixing antigens were obtained for at least one member of each antigenic group tested. Ehrlich ascitic tumor was compared with sarcoma 180 as a source of antigens; although sarcoma 180 showed many advantages over Ehrlich tumor, the latter gave, in general, better results for complement-fixing antigens. Oncolytic effect with complete recovery of the mice was observed in some instances. The highest recovery rate resulted with Congo and UNA viruses (40%), and the second highest rate resulted with dengue 2, St. Louis, Hazara, and Uukuniemi viruses (20%). The best survival was observed, in decreasing order, with Congo, St. Louis, dengue 2, Tacaribe, Sindbis, Junin, and Amapari viruses. (Author abstract) (10 Refs)

32. PURIFICATION OF POLYOMA VIRUS MEDIUM-SIZE TUMOR ANTIGEN BY IMMUNOAFFINITY CHROMATOGRAPHY.

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Proc Natl Acad Sci USA; 79(13):4025-4029 1982

We have used antibodies against the synthetic peptide Lys-Arg-Ser-Arg-His-Phe, corresponding to the six COOH-terminal amino acids of the polyoma virus medium tumor (T) antigen, to purify the medium T antigen by affinity chromatography. Release of the medium T antigen from the anti-peptide antibody was achieved under mild conditions by using a large excess of the peptide in an isotonic buffer at neutral pH containing mixed detergents. This procedure yielded a 2,500-fold purification of the medium T antigen in a single step. The protein kinase activity associated with the medium T antigen was also released and was studied in this active state in solution. Sedimentation analysis showed that the bulk of the purified medium T antigen was in a monomeric form (Mr about 42,000) not associated with protein kinase activity. A small fraction of the medium T antigen was found in a rapidly sedimenting form (Mr about 200,000) that possessed protein kinase activity. (Author abstract) (26 Refs)

33. THE BINDING OF SIMIAN VIRUS 40 LARGE T ANTIGEN TO THE POLYPHOSPHATE BACKBONE OF NUCLEIC ACIDS.

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Biochim Biophys Acta; 697(3):322-329 1982

Simian virus 40 (SV40) large tumor antigen (T antigen), a phosphoprotein found in nuclei of SV40-infected and -transformed cells, binds nonspecifically to DNA. To study this mechanism the binding properties of T antigen to double-stranded (ds) and single-stranded (ss) DNA-cellulose as well as to phosphocellulose were compared. After incubation of [35S]methionine or [3H]leucine/[32P]phosphate radioactively-labeled cell extracts at different pH values (6.0, 7.3, 9.0) with DNA- or phosphocellulose, bound and unbound species of T antigen were purified and analyzed by SDS-polyacrylamide gel electrophoresis for both the yield and the possible correlation with protein phosphorylation. T antigens bound with comparable affinities to ds- and ss-DNA-cellulose and phosphocellulose. These results suggest the binding of T antigen to the polyphosphate backbone of DNA as a molecular mechanism for its nonspecific binding. The evidence for this observation was supported by blocking the binding of T antigen to DNA-cellulose by divalent cations (Ca++, Mg++). 3H/32P ratios of T antigen obtained by double-labeling cells for various times imply that higher phosphorylated forms of T antigen bound more strongly to ds- and ss-DNA as well as to phosphocellulose. Thus, in the presence of cellular proteins and other components the binding activity of T antigen to the polyphosphate backbone of DNA seems to be positively correlated with its phosphorylation. These observations are consistent with the hypothesis that the binding affinities of SV40 T antigen to host cell DNA may be regulated by its phosphorylation. (Author abstract) (24 Refs)

TUMOR ASSOCIATED TRANSPLANTATION ANTIGENS

34. AUGMENTED IMMUNOGENICITY OF LEWIS LUNG CARCINOMA BY INFECTION WITH HERPES SIMPLEX VIRUS TYPE 2.

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Eur J Cancer Clin Oncol; 18(6):523-531 1982

In vitro, LLT cells sustain HSV-2 replication without evidence of lysis. Simultaneously, multiplication of the cells is stimulated. These xenogenized cells were tested for their immunopotentiating capacity: three-step immunization with xenogenized viable cells conferred significantly augmented transplantation resistance to a challenge graft with 4 x 10(4) intact LLT cells. Latency periods preceding tumor formation were increased and 15% of the mice failed to form primary tumors. Metastasis was likewise decreased and 25% of the mice had healthy lungs. Immunopotentiation, however, did not suffice to significantly protect against a challenge with 6 x 10(4) intact cells. The presence of virus-specific neoantigens on HSV-2-infected viable cells was demonstrated by the progressively increasing number of rejections of 4 x 10(4) xenogenized cells during the successive immunization steps. Immunization with non-viable LLT cells did not augment resistance to challenge. (Author abstract) (31 Refs)

35. PURIFIED MEMBRANE FRACTIONS FROM MAMMARY TUMOR CELLS ELICIT BIOLOGICAL REACTIVITY IN IN VITRO CELL-MEDIATED IMMUNE REACTIONS.

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Eur J Cancer Clin Oncol; 18(6):595-604 1982

Lithium chloride (LiCl) aggregation followed by centrifugation through a sucrose step gradient was used to obtain purified plasma membranes from two sublines of mouse mammary adenocarcinoma. These two tumor lines were chemically induced by treatment of a hyperplastic nodule with 7,12-dimethylbenzanthracene (DMBA). One line, D1-DMBA-3, has been found to be immunogenic to the host of origin, while the other, D1-DMBA-2, does not elicit specific tumor immunity as previously tested in in vivo and in vitro immune reactions. The purified membrane fractions were assayed for protein, DNA and sialic acid content as well as enzymatic markers of membrane purity. When tested in blastogenesis and cytotoxicity reactions, membrane-containing fractions from the D1-DMBA-3 immunogenic tumor were found to be stimulatory to spleen cells of D1-DMBA-3 tumor bearers over a 10-fold protein concentration. Spleen cells from normal mice do not respond in these reactions to the various tumor fractions. No reactivity was observed when non-membrane-containing preparations were used as stimuli in the cell-mediated immune reactions. The specificity of these reactivities was further demonstrated by the lack of responses when fractions from the non-immunogenic D1-DMBA-2 tumor were tested in parallel in our in vitro assay. The data presented indicate that the procedure employed is useful for the isolation of membrane-associated, tumor-specific antigens which can be easily quantitated and still retain biological activity in in vitro tests of cell-mediated immunity. (Author abstract) (41 Refs)

36. ADOPTIVE CHEMOIMMUNOTHERAPY OF A SYNGENEIC MURINE LYMPHOMA WITH LONG-TERM LYMPHOID CELL LINES EXPANDED IN T CELL GROWTH FACTOR.

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Cancer Immunol Immunother; 13(1):5-13 1982

The cure of disseminated syngeneic FBL-3 lymphoma in female C57/BL/6 mice was attempted with the use of in vivo-immunized cells, in vitro-sensitized cells, whole lymphoid populations expanded in T cell growth factor (TCGF), and with cloned cytotoxic cells expanded in TCGF. In 3/3 experiments, 20/38 mice receiving cytoxan (CY) plus in vivo-immunized lymphoid cells were cured of tumor compared to 0/31 mice treated with CY plus normal lymphocytes. In vivo-immunized lymphocytes were resensitized to irradiated FBL-3 tumor in complete medium (CM) or lectin-free TCGF (LF-TCGF). In the CM group 41/50 animals were cured. In the LF-TCGF group 36/61 animals were cured. No significant difference was observed in the in vivo effects of cells in vitro sensitized (IVS) in CM or LF-TCGF. IVS cells were resensitized in vitro to irradiated FBL-3 tumor for 5 days. Simultaneously, normal C57BL/6 lymphocytes were co-cultured with normal C57BL/6 irradiated stimulators. Neither of these groups showed significant lysis of fresh FBL-3 tumor in an 18-hr 51Cr-release assay in six of eight experiments. Treatment of mice with CY plus immune lymphocytes sensitized to normal C57BL/6 stimulators and then expanded in LF-TCGF resulted in no increase in survival compared with CY alone. Treatment of mice with CY plus immune lymphocytes resensitized to FBL-3 tumor in vitro and expanded in LF-TCGF cured 7/27 animals and prolonged survival over that in all control groups. Treatment with CY plus normal nonimmune lymphocytes resensitized to normal C57BL/6 stimulators and expanded in LF-TCGF for 2.5 mo did not prolong survival compared with CY controls. CY plus immune lymphocytes sensitized to FBL-3 tumor and expanded continuously in LF-TCGF for 2.5 mo showed marked prolongation of survival and cured 5/9 mice. Implications of results for application of these techniques to other less antigenic tumors and human cancers are discussed. (49 Refs)

37. CLONAL ANALYSIS OF EXPRESSION OF TUMOR-ASSOCIATED TRANSPLANTATION ANTIGENS AND OF METASTATIC CAPACITY.

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Cancer Immunol Immunother; 13(1):62-68 1982

Heterogeneity of two tumor lines, Eb, a subline of the methylcholanthrene-induced DBA/2 lymphoma L5178Y, and ESb, a spontaneous metastatic variant of Eb, was investigated with respect of expression of tumor antigens and Fcgamma receptors, and metastatic potential. Twenty-six of 28 Eb clones were recognized and killed in the 4-hr 51Cr assay by anti-Eb cytolytic T lymphocytes (CTL). All 32 clones from the metastatic variant ESb were recognized by anti-ESb CTL, while none reacted significantly with CTL raised against the parental line. While all ESb clones were Fcgamma receptor-positive and formed rosettes in the range of 60%-90%, all the Eb clones were negative in the antibody-coated sheep erythrocytes rosette assay. Typing results of analysis of six Eb clones showed that cloned tumor cell lines can vary considerably in the sensitivity to specific antitumor cytotoxic cells. When uncloned Eb or ESb tumor cells were tested in vivo for growth and metastatic capacity in syngeneic animals a considerable variability was noted between individual mice within the same experimental group. The majority of clones showed variability of local sc growth similar to that observed with the uncloned ESb population. Only high malignant lines (like ESb-Cl 50) were found to grow, metastasize, and kill the hosts in a reproducible manner. Values for the 50% and 100% mortality times for 52 ESb clones and for the uncloned Eb and ESb populations showed differences in the overall metastatic potential between individual clones. (29 Refs)

38. AN EXAMINATION OF ADENOVIRUS TYPE 5 MUTANTS FOR THEIR ABILITY TO INDUCE GROUP C ADENOVIRUS TUMOR-SPECIFIC TRANSPLANTATION ANTIGENICITY IN RATS.

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Virology; 120(1):146-156 1982

The expression of Group C adenovirus tumor-specific transplantation antigenicity (TSTA) has been examined in rats using a variety of Type 5 adenovirus (Ad-5) mutants. Transformation-defective Group I E1A mutants (other than Ad-5 hr1 and hr2), Group II E1B mutants, and N gene mutants, produced significantgly lower TSTA or no TSTA when compared with levels of TSTA induced by Ad-2 and Ad-5 wild-type viruses. Two mutants, Ad-5 sub304 and Ad-5 ts125, neither of which possess lesions within the transforming sequences, induced high levels of TSTA in vivo. (Author abstract) (43 Refs)

CLINICAL DIAGNOSTIC STUDIES

39. ULTRASTRUCTURAL PEROXIDASES AND IMMUNOLOGICAL MARKERS IN ACUTE ADULT LEUKEMIA: THERAPEUTIC APPLICATIONS.

Marie JP, Escribano L, Perrot JY, Boucheix C, Kayibanda M, Martyre MC, Cadiou M, Rosenfeld C, Zittoun R
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Nouv Presse Med; 11(21):1603-1606 1982

In a retrospective study of 112 adult patients with acute leukemia (AL), the percentage of undifferentiated leukemia was reduced to almost 1% by an analysis of routine cytochemical reactions (PAS, peroxidase, esterases and esterase inhibition), B and T lymphocyte markers (IgS, E-rosettes, HuTLA) cALL antigen and ultrastructural detection of peroxidase activity (PO-ME). A simultaneous study of cALL antigen and PO-ME showed reciprocal exclusion of these markers, except in one case of mixed leukemia. Therapeutically, the value of these tests lies in that patients with typical PAS reaction and cALL antigen consistently respond to vincristine-corticosteroid treatment, whereas patients without cALL and with PO-ME are frequently resistant to that combination of drugs. (Author abstract) (15 Refs) (In FRE)

40. THE IMMUNOLOGICAL CLASSIFICATION OF LEUKAEMIA BASED ON A RAPID MICROCYTOTOXICITY TEST.

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Clin Exp Immunol; 49(1):142-148 1982

We describe a rapid, accurate, and reproducible cytotoxic antibody test for the immunological classification of leukemia. Well characterized heteroantisera and monoclonal antibodies were distributed in a microcytotoxicity tray referred to as a leukemia screening tray (LST). Leukemia cells were tested for the presence of Ia-like, 'blast', thymocyte, common acute lymphoblastic leukemia (cALL), and acute myeloblastic leukemia (AML) antigens. Utilizing this technique, T ALL could be distinguished from non-T ALL, ALL and AML could be differentiated, the myeloid blast crisis of chronic myelogenous leukemia (CML) could be distinguished from the lymphoid blast crisis, and the T lymphocyte and B lymphocyte lymphoid leukemias were readily identified. It has been shown that subclassification of leukemia according to surface markers, as described here, offers considerable improvement in the diagnosis and treatment of leukemia over the classical morphological methodologies. Because the test can be completed in 2 hr and unlimited amounts of monoclonal antibodies are available, the LST or similar tests should become universally available in the future to supplement morphological data and replace other lengthy enzyme and rosetting tests. (Author abstract) (34 Refs)

41. IMMUNOLOGICAL MARKERS OF LANGERHANS' CELLS IN MYCOSIS FUNGOIDES SKIN LESIONS.

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Acta Derm Venereol (Stockh); 62(3):241-243 1982

The patterns of two immunological markers of epidermal Langerhans' cells were compared in normal skin and mycosis fungoides (MF) skin lesions. A double-staining indirect immunofluorescence method was used. Cells suggestive of keratinocytes reacted with the anti-Ia antibodies in some cases of MF lesions, while no such pattern was seen with the thymocyte-antigen antibodies (OK T6). In other cases of MF, as in normal skin, the epidermal picture was mainly the same with the two markers. A great many of the dermal mononuclear cells in MF were reactive with the anti-Ia antibodies but only occasional dermal cells in MF and no dermal cells in normal skin stained with OK T6. (Author abstract) (14 Refs)

42. IMMUNOLOGY AND DIAGNOSIS OF NASOPHARYNGEAL CARCINOMA.

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Excerpta Med Int Congr Ser; 571:389-397 1982

Results of a series of studies are discussed to assess the value of testing for some Epstein-Barr virus (EBV)-specific serologic and immunologic markers in the diagnosis of nasopharyngeal cancer (NPC). All the sera tested were from Chinese patients and residents in Hong Kong. The sera were titrated for IgA and IgG antibodies to viral capsid antigen (VCA) and early antigen (EA) of EBV by the indirect immunofluorescent technique. The first study showed that NPC patients have a broader spectrum and higher geometric mean titer (GMT) of serum antibodies to EBV-specific antigens than do patients with other tumors of the respiratory and upper aerodigestive tracts and healthy subjects. A second study established that there was a stepwise rise in the GMT for all four antibodies with advancing stages of disease (I-IV). A further study was done to assess the value of titration of the four antibodies in the diagnosis of NPC. IgA to VCA had the highest sensitivity with a detection rate of 95% and relatively high specificity. IgA to EA was highly specific with no false positives but a detection rate of only 78%. IgG to VCA was the least discriminatory, while EgG to EA fell between IgA to EA and IgG to VCA. An ongoing study involves the evaluation of the titration of serum IgA to VCA as a screening test for NPC in its early presymptomatic stage in subjects known to have a high risk of the disease, namely, close blood-linked relatives of Chinese NPC patients. In these patients, if the serology is suggestive, multiple nasopharyngeal biopsies are indicated. Data are presented on serum EBV-specific antibody titers in four siblings initially and at time of diagnosis of NPC. (17 Refs)

43. SEROLOGICAL STUDIES ON NASOPHARYNGEAL CARCINOMA AND CERVICAL CANCER IN CHINA.

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Excerpta Med Int Congr Ser; 571:380-388 1982

A serological study on Epstein-Barr virus (EBV) infection was performed in areas of high and low risk for nasopharyngeal cancer (NPC). A micro-complement fixation test for antibody to EBV in sera of 2,300 normal individuals of all ages indicated a positive reaction in 90-100% of children aged 3-5 yr. The geometric mean titer (GMT) from the healthy population over age 20 was significantly higher in areas of high NPC risk. This type of variation may reflect reactivation of EBV in people living in the NPC high risk area and which might be related to the occurrence of NPC. Results of serologic mass surveys of NPC are reported in Zangwu county in 1978-1980. The incidence of antibody to herpes simplex virus (HSV) 1 and 2 was determined in normal women in both a high- (Jienan county) and a low-risk (Beijing) area for cervical cancer and in patients. There was no marked difference in frequency of antibody to HSV-1 in the cervical cancer patients and in the controls from high and low risk areas. However, in the cervical cancer group, the GMT of antibody to HSV-1 was a little higher than that in the control group; this may be due to cross-reaction to antigen between HSV-1 and HSV-2. A study of age-specific incidence of HSV infection in areas of high and low cervical cancer risk indicates a relationship between early and severe infection of HSV-2 and high risk of cervical cancer. While the age-specific incidence of HSV-2 infection in China is similar to that in some western countries, the social system and life-style are quite different, indicating some other mode of infection than venereal transmission. (22 Refs)

44. NASOPHARYNGEAL CARCINOMA AND CERVICAL CARCINOMA IN TAIWAN, CHINA.

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Excerpta Med Int Congr Ser; 571:398-407 1982

Some epidemiological studies on nasopharyngeal cancer (NPC) and cervical cancer (CC) in Taiwan are presented; possible association with oncogenic viruses is also discussed. Epidemiological data presented are based on surveys since neoplasms are not reportable in Taiwan. The age-standardized death rate (per 100,000 of population) for NPC in 1979 was 3.3 (4.6 for males, 1.9 for females). As in other countries, the rate was higher in the Chinese population. The death rate has increased slightly during the past 15 yr. Morbidity incidence from 1969-1971 of NPC was estimated at 5.4. Patients with NPC show a significantly higher anti-virus capsid antigen (VCA) titer than neighborhood controls, their families, and NPC family members. A synergistic interaction with NPC was found between all pairs of factors of smoking, ventilation, nasal balsam or oil, herb drugs, and anti-VCA titer, except that between herb drugs and ventilation. The age standardized death rate (per 100,000 of female population) for CC in 1979 was 6.9, which ranked CC fourth among causes of death in females. The death rate due to CC increased markedly after age 40 yr. CC death rates were higher in those who were ever married, compared with those who were single, widowed, or divorced. (6 Refs)

45. MONOCLONAL ANTIBODIES AGAINST SURFACE ANTIGENS OF LARYNGEAL CARCINOMA CELLS. A NEW EXPERIMENTAL APPROACH FOR THE EARLY DIAGNOSIS AND IMMUNOTHERAPY.

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Excerpta Med Int Congr Ser; 582:141-146 1982

Use of monoclonal antibodies against surface antigens of laryngeal carcinoma cells as an approach for early diagnosis and immunotherapy is reported. The outer cell membranes of tumor cells can be broken down in their protein components by polyacrylamide gel electrophoresis. A radioimmunoassay was used to demonstrate that 47/50 laryngeal cancer patients formed antibodies to their own tumors. Of 52 patients examined, 20% possessed IgG-antibodies which cross reacted with the isolated carcinogenic cells from a single patient. A model of surface antigens in laryngeal carcinomas was proposed. Most surface antigens can be detected in both normal and malignant cells, however, tumor cells lack certain surface characteristics; other antigens are found only in tumor cells. Xenogeneic antibodies were used to prepare monoclonal antibodies for clinical studies. Clones were produced from myeloma cells crossed with antibody producing splenic cells. Seventy-three clones capable of forming anti-laryngeal antibodies were identified. The monoclonal antibody identifies various malignant target cells, including two laryngeal carcinomas and two salivary gland carcinomas. Immunofluorescence studies demonstrated that the monoclonal antibodies used can differentiate tumor tissue from non-tumor tissue. Using monoclonal antibodies as reported groups, a single cell which is not identifiable as malignant or not could be shown to possess antigens corresponding to the serum. (5 Refs)

46. THE IMMUNOHISTOCHEMICAL REACTIVITY OF A HUMAN MONOCLONAL ANTIBODY WITH TISSUE SECTIONS OF HUMAN MAMMARY TUMORS.

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Cancer; 50(2):241-249 1982

Human monoclonal antibodies have been generated following the fusion of human lymphocytes (obtained from axillary lymph nodes of mastectomy patients) with a murine nonimmunoglobulin secreting myeloma cell line. We report a detailed analysis of the reactivity of a human IgM monoclonal antibody secreted by one of these double cloned hybridoma cell lines. Tissue sections of both malignant and benign human mammary tumors, as well as apparently normal tissues, were tested using the immunoperoxidase technique and the human monoclonal antibody. Eighty-one per cent (54/67) of primary malignant mammary tumors, 100% (20/20) of metastatic breast lesions, and 14% (3/22) of benign breast lesions reacted positively with a moderate or strong intensity. The per cent of mammary carcinoma cells that stained and the pattern of staining varied among different tumor samples. While reactivity was observed with selected carcinomas of nonbreast origin, little or no reactivity was observed with apparently normal human tissues including normal mammary epithelium. The antibody reactivity observed was shown to be clearly distinct from those of both anti-T and anticarcinoembryonic antigen sera. (Author abstract) (19 Refs)

47. PREOPERATIVE AND POSTOPERATIVE REACTIVITY OF BREAST CANCER PATIENTS AGAINST TUMOR-ASSOCIATED ANTIGENS AND HEP IN THE MACROPHAGE-ELECTROPHORETIC-MOBILITY (MEM) TEST.

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Arch Geschwulstforsch; 52(6):469-78 1982

Fifty women, including 27 with breast cancer (BC) and 23 with benign diseases of the breast, were tested preoperatively by the macrophage-electrophoretic-mobility (MEM) test. Patients with BC included five with a second BC occurring several yr after ablation of the contralateral breast. Patients with benign diseases included 21 with benign tumors (16 fibrocystic mastopathies, 2 fibroadenomas, 1 foam-cell granuloma, 1 intracanalicular papilloma, and 1 lipoma). Patients with BC were tested 4-7 days, 5-8 wk, and 11-20 wk postoperatively. In all tests, MEM tests were conducted in the presence of human encephalitogenic protein (HEP), 3 M KCl extract of BC tissue, or 3 M KCl extract of renal carcinoma (RC). A total of 289 tests were conducted on 102 blood samples from 50 patients. Preoperative diagnosis by the MEM test had an accuracy of 89%, a sensitivity of 86%, and a selectivity of 91% with BC extract; with HEP the accuracy was 86%, the sensitivity 75%, and the selectivity 95%. With RC extract, positive results were obtained in only 3% of tests; the selectivity was 97%, indicating that the MEM test is organ-specific. In BC patients, reactivity to HEP and BC extract was not immediately affected by surgery. Reactivity declined sharply 5-8 wk after surgery. In some patients reactivity later increased, suggesting a recurrence of BC. Inhibition of lymphocytic migration showed two nonoverlapping groups, one with values near 0% and one with values near 10%. The MEM test using HEP or BC extract as the antigen is evidently useful for differentiation of benign and malignant breast disease and for follow-up of BC. (32 Refs) (In GER)

48. IMMUNITY IN PATIENTS WITH KIDNEY CANCER.

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Urological Clinic, Byelorussian Inst. Advanced Training for Physicians, Minsk, USSR
Urol Nefrol (Mosk); (3):16-20 1982

The state of antitumor immunity was studied in 95 patients with primary kidney cancer (Group 1), 19 patients with postoperative metastases or recurrences of kidney cancer (Group 2), and in 33 clinically cured patients (Group 3). The patients in Groups 1 and 2 showed progressive decrease of leukocyte and lymphocyte counts and increase of monocyte count. The patients in Group 3 had normal leukocyte and lymphocyte counts and elevated monocyte count. Skin tests showed reduced reaction to phytohemagglutinin (PHA), tuberculin, and embryonal antigen and increased reaction to tumor-associated antigen in the patients in Groups 1 and 2, while the patients in Group 3 had normal response to PHA and tuberculin and lack of response to embryonal and tumor-associated antigens. The changes in the functional activity of the immunocompetent cells depended upon the stage of the disease. The decrease of the indices of cellular immunity was associated with stage-dependent elevation of parameters of humoral immunity. (11 Refs) (In RUS)

49. IMMUNOHISTOCHEMISTRY OF PROSTATIC ACID PHOSPHATASE.

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Ann NY Acad Sci; 390:133-141 1982

The use of the immunoperoxidase reaction for prostate specific acid phosphatase (PSAP) as a practical, sensitive, and specific test for evaluating the possible prostatic origin of otherwise unclassifiable primary or metastatic tumors is reported. Any positive staining should be regarded as evidence for prostatic origin of a given tumor. By pooling several monoclonal antibodies raised against different antigenic determinants of prostatic acid phosphatase, the sensitivity of the reaction can be enhanced. In sections of normal and hyperplastic prostate glands, only the epithelium of prostatic acinar glands and ducts and prostatic secretions and concretions stained positively for PSAP. Positive results may also be seen in the prostate glands of fetuses on the luminal border of a few glandular cells. Compared with positive staining observed in greater than 250 cases of known primary or metastatic prostatic carcinomas, none of the greater than 120 cases of nonprostatic malignancies demonstrated immunohistochemical staining for PSAP. The intensity of the reaction may vary considerably from cell to cell, area to area, and from primary to metastatic tumor in the same patient. All primary and metastatic prostatic malignancies reacted positively to a human prostate-specific antigen, while nonprostatic neoplasms did not. Before the immunoperoxidase reaction for PSAP is used for diagnostic purposes, the specificity of antibody and sensitivity of the technique should be well defined. (18 Refs)

OTHER RELATED STUDIES

50. BYSTANDER SUPPRESSION OF TUMOR GROWTH: EVIDENCE THAT SPECIFIC TARGETS AND BYSTANDERS ARE DAMAGED BY INJURY TO A COMMON MICROVASCULATURE.

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J Immunol; 129(2):890-899 1982

The immune response to certain tumors can also suppress the growth of antigenically distinct (bystander) tumor cells injected at the same site. In some cases, bystander suppression occurs during the course of the primary but not the anamnestic response to the same neoplastic cells. We analyzed the pathogenesis of bystander suppression in strain 2 guinea pigs by studying the host response to mixtures of different syngeneic and allogeneic tumors. In nonimmune animals, intradermal injection of syngeneic line 1 hepatoma cells was associated with extensive proliferation of fibroblasts and small blood vessels at the tumor periphery, a host response that provided the tumor with a vascularized stroma and invested it in a broad zone of host connective tissue. Syngeneic line 10 hepatoma cells also induced a vascular stroma but elicited less fibroblast proliferation and a more sparse leukocytic infiltrate. The microvasculature of line 10 tumors exhibited minimal endothelial damage and large regions of tumor necrosis did not occur; these neoplasms grew progressively, metastasized, and killed the host. Tumors composed of mixtures of line 1 and line 10 cells evoked a host response identical to that elicited by line 1 tumors. The anamnestic response to line 1 cells and the primary or anamnestic responses to allogeneic tumors differed from the primary response to line 1 tumor in two important respects: lymphocytes, basophils, and other inflammatory cells accumulated rapidly and achieved intimate contact with neoplastic cells; and destruction of specific tumor cells was effected promptly, limiting the development of a significant host connective tissue and vascular response. Under such circumstances, line 10 cells escaped nonspecific destruction and grew progressively. (33 Refs)

51. EVALUATION OF A TISSUE TRANSPORT MEDIUM FOR IMMUNOLOGICAL CHARACTERIZATION OF BENIGN AND MALIGNANT LYMPHOID TISSUES.

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A tissue transport medium was evaluated for its usefulness in immunologic characterization of lymphocytes in tissue sections. A variety of lymphoid tissues were studied, including normal tissue, hyperplastic tissue and malignant lymphoma. Approximately equal parts of biopsy samples were taken and one part was immediately snap-frozen while the other was held in transport medium for up to 1 week before processing for frozen section. Sections were stained with fluorescein-conjugated anti-immunoglobulin antisera and with a variety of murine monoclonal antibodies to T-cell antigens or Ia antigen followed by staining with fluorescein-conjugated goat-antimouse gamma globulin. In all cases studied, there was complete agreement in the staining patterns of tissues which were either immediately snap-frozen or held in transport medium. (Author abstract) (19 Refs)

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